
National Institute on Drug Abuse
Director's Report
to the
National Advisory Council on Drug Abuse
May, 1999

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****May, 1999**

Research Findings

Basic Research

Dopamine and Reward

The operation of a circumscribed reward system in which dopamine accumulation in the nucleus accumbens is appreciated as a reward is a key concept underlying substance abuse research. This concept evolved from two observations: 1) most drugs of abuse and natural rewards elicit the accumulation of dopamine in the accumbens, and 2) animals will self-administer electrical impulses to areas of their brains that closely correspond to catecholaminergic projections. The results of a newly published study raise questions about this interpretation of the actions of dopamine. Wightman and his colleagues used voltametry to measure the extracellular dopamine in the nucleus accumbens after intracranial electrical stimulation in rats. The stimulation was delivered either by the rats themselves, or by the experimenter without regard to the rats' behavior. Wightman found that: 1) rats were unable to learn to self-stimulate if the stimulation produced no dopamine release; 2) experimenter-delivered stimulation reliably increased the dopamine accumulation in the accumbens in animals that could learn the task; and 3) unexpectedly, once the task was learned, little dopamine accumulated as the animal self-administered the stimulation. By using a method with better temporal resolution than that available with microdialysis, Wightman demonstrated that the release of dopamine may not be critical in reinforcement once the task is learned. These findings also suggest that the dopaminergic response may evolve as an alerting function in response to novelty or as a predictor of reward. Garris, P.A., Kilpatrick, M., Bunin, M.A., Michael, D., Walker, Q.D., and Wightman, R.M. *Nature* 398, pp. 67-69, 1999.

Neuronal Nitric Oxide Is Involved in Cocaine Reward

Dr. Yossef Itzhak led studies to investigate the role of nitric oxide (NO) in the rewarding property of cocaine. Mice treated with cocaine every other day and saline on the alternate days for 8 days developed conditioned place preference (CPP) for the cocaine-paired compartment of the cage. Treatment with the neuronal NO synthase (nNOS) inhibitor 7-nitroindazole prior to each cocaine injection completely blocked cocaine CPP. Further, homozygote nNOS(-/-) knockout mice (i.e. mice lacking the nNOS gene) did not develop preference for the cocaine-paired compartment following the administration of cocaine, while wild-type nNOS(+/+) mice developed marked cocaine CPP. Thus, both pharmacologic and genetic manipulations of nNOS suggest that NO is involved in the rewarding property of cocaine. Itzhak, Y., Martin, J.L., Black, M.D., and Huang, P.L. *NeuroReport*, 9(11), pp. 2485-2488, 1998.

The Neuroendocrine Protein 7B2 Is Required for Peptide Hormone Processing In Vivo and Provides a Novel Mechanism for Pituitary Cushing's Disease

The neuroendocrine protein 7B2 is widely distributed within endocrine and neural tissues. It is absolutely required for the production of active prohormone convertase 2 (PC2), an important neuroendocrine precursor processing endoprotease. NIDA grantee Iris Lindberg of Louisiana State University Medical Center and her coworkers, in collaboration with researchers at Harvard, report the creation of 7B2 knockout mice. These animals have no PC2 activity, thus providing an in vivo confirmation of the requirement of PC2 for the 7B2 protein. Like PC2 knockout mice, the 7B2 knockout mice exhibit deficient processing of islet hormones and altered pancreatic islet morphology, and are hypoglycemic, hyperproinsulinemic and hypoglucagonemic. In contrast to the PC2 knockout mice, however, these mice show markedly elevated circulating adrenal corticotrophic hormone (ACTH) and corticosterone levels, with expansion of the adrenal cortex. Before they are 9 weeks old 7B2 knockout mice die of severe Cushing's disease as a consequence of ACTH hypersecretion from the intermediate lobe of the pituitary. Therefore, 7B2, required for activation of the processing enzyme PC2, has additional important functions in the regulation of secretion of pituitary hormones, and 7B2 knockout mice can provide a new avenue for the exploration of the regulation of peptide secretion. Westphal, C., Muller, L., Zhou, A., Zhu, X., Bonner-Weir, S., Schambelan, M., Steiner, D., Lindberg, I., and Leder, P. *Cell*, 96, pp. 689-700, 1999.

Orphanin-FQ/Nociceptin (OFQ/N) Modulates the Activity of Suprachiasmatic Nucleus Neurons

Circadian rhythms characterized by regular daily fluctuations in behavioral and physiological processes are regulated by the suprachiasmatic nucleus (SCN), a structure located above the optic chiasm of the ventral hypothalamus. Alterations in the duration of light modify circadian rhythms by influencing the patterns of activity of the SCN through NMDA receptor-mediated calcium influx. Increases in intracellular calcium activate nitric oxide synthase to produce nitric oxide, which activates cGMP and alters neuronal activity. Researchers at Oregon Health Sciences University have discovered the presence of the Orphanin-FQ/Nociceptin receptor, a receptor sharing homology with the opioid receptors and its ligand orphanin FQ in the SCN. To test whether OFQ/N plays an important role in regulating circadian rhythms, OFQ/N was unilaterally injected into the SCN of Syrian hamsters. OFQ/N inhibited the light-induced phase shifts of the onset of wheel running activity but did not directly phase shift the circadian clock. OFQ/N appears to attenuate the light induced phase shifts of the circadian clock by directly inhibiting NMDA receptor mediated calcium influx, and indirectly inhibiting the activation of NMDA receptors in the SCN by activating a potassium current that hyperpolarizes SCN neurons. Hyperpolarization prevents glutamate from activating the NMDA receptor. The effects of OFQ/N were blocked by OFQ/N antagonists but not by naloxone suggesting that OFQ/N acts through a unique non-opioid receptor. Allen, C.N., Jiang, Z.G., Teshima, K., Darland, R., Ikeda, M., Nelson, C.S., Quigley, D.I., Yoshioka, T., Allen, R.G., Rea, M.A., Grandy, D.K. *Journal of Neuroscience*, 19, pp. 2152-2160, 1999.

Endomorphin Conformation

An analysis of the conformations of the endogenous mu-selective ligand endomorphin-1 has been carried out by a collaborative study involving NIDA-funded researchers Dr. David M. Ferguson and Dr. Maria G. Paterlini of the University of Minnesota. Results of solution nuclear magnetic resonance (NMR) and molecular modeling simulation suggest the existence of a major "extended" conformation lacking internal hydrogen bonds. After aligning the respective tyrosines (the so-called "message" region involved in producing the ligand's opioid effect) of endomorphin-1 with the mu-selective ligands PL-017 and TIPP, reasonably good overlap was seen in the "address" regions (the third amino acid of each) believed to be involved in conferring mu-selectivity. The same region of overlap was not seen in comparing endomorphin-1 with the delta-selective ligand DPDPE and the mu/delta ligand TIPP-Nh3. Further studies will elucidate the structure-function relationships in the endomorphins. Podlogar, B.L., Paterlini, M.G., Ferguson, D.M., Leo, G.C., Demeter, D.A., Brown, F.K., and Reitz, A.B., *FEBS Letters* 439(1-2), pp. 13-20, 1998.

Peptide Prodrugs

In a recent collection of reports, Dr. Ronald Borchardt and his associates have described efforts to improve the membrane permeability and stability of opioid peptides Leu-enkephalin and DADLE (H-Tyr-D-Ala-Gly-Phe-D-Leu-OH). This was accomplished by converting them into various cyclic prodrugs, and examining their passage across an in-vitro cellular model of the intestinal mucosa, and their stability toward chemical and enzymatic cleavage. In the case of coumarinic acid-based prodrugs, enhanced bi-directional permeation was demonstrated in the cellular model as compared to the peptides themselves. It was possible to demonstrate separately in buffered solution the formation of a non-cyclic intermediate, and subsequent quantitative release of the parent peptide and coumarin. In the case of acyloxyalkoxy-based prodrugs, the permeation was largely unidirectional, suggesting that these prodrugs were a substrate for an efflux transporter, such as P-glycoprotein. In all cases, considerably shorter half lives for the

prodrugs were found upon exposure to rat liver and plasma enzymes, which fairly rapidly cleave the prodrug to the peptide and subsequently hydrolyze the peptide. This work points out some of the practical considerations in the design of delivery systems capable of transporting and delivering peptides of therapeutic interest, particularly to enhance their oral bioavailability. Bak, A., Gudmundsson, O.S., Pauletti, G.M., Shan, D., Wang, W., Siahaan, T.J., Friis, G.J., Wang, B., Shan, D., Zhang, H., and Borchardt, R.T. *Pharmaceutical Research*, 16, pp. 7-29, 1999.

Anandamide May be Involved in the Response of the Immune System to Cannabinoids

Dr. Burstein and his colleagues have examined whether the capacity of agents to mobilize arachidonic acid (AA) could predict increased anandamide (ANA) synthesis in a macrophage cell line. Lipopolysaccharide (LPS), platelet-activating factor (PAF), and cannabinoids such D9-tetra-hydrocannabinol (THC) and ANA were all found to be agonists for the release of AA and led to increased ANA synthesis in macrophage cells for the mouse cell line RAW264.7. Nitric oxide, in contrast, stimulated AA release without raising ANA levels. ANA stimulation of its own synthesis indicates the existence of a positive feedback mechanism. ANA synthesis is also increased by the combination of calcium ionophore and indomethacin, suggesting that ANA is metabolized by a cyclooxygenase in this system. These data imply that ANA could play a role in the response of the immune system to cannabinoids and bacterial endotoxins and that AA mobilization is a predictor for increased ANA synthesis. Pestonjamas, V.K., and Burstein, S.H. *Biochimica et Biophysica Acta* 55325, pp. 1-12, 1998.

3,4-Methylenedioxymethamphetamine (MDMA or "ecstasy") Induced Acute Changes in Dopamine (DA) Transporter Function

The acute effects of the amphetamine designer drug, MDMA, on dopamine (DA) transporter function in rat striatum were investigated and compared to other psychostimulants known to influence monoaminergic systems. A single MDMA injection (10-20 mg/kg; sub-cutaneously (s.c.)) caused a dose-related decrease in [3H]dopamine uptake into striatal synaptosomes prepared one hour after MDMA injection. This rapid effect on [3H]dopamine uptake returned to control levels 24 hours after treatment. A single administration of other amphetamine analogs, such as methamphetamine (15 mg/kg; s.c.), p-chloroamphetamine (10 mg/kg; intra-peritoneally (i.p.)) or methcathinone (30 mg/kg; s.c.), also rapidly decreased striatal [3H]dopamine uptake. In contrast, a single or multiple administrations of cocaine (30 mg/kg; i.p.) had no effect on [3H]dopamine transport into striatal synaptosomes. These changes in dopamine transporter activity by the amphetamine analogs may occur via reactive oxygen species-mediated mechanisms. The results obtained implicate novel mechanisms by which the DA transporter can be regulated pharmacologically as well as physiologically, and further demonstrate a newly observed effect of amphetamine analogs on dopaminergic neurons. Since the normal function of the DA transporter is to regulate the action of released DA, disruption of DA transporter function can lead to deleterious effects such as changes in dopaminergic transmission and behavior. Metzger, R.R., Hanson, G.R., Gibb, J.W., Fleckenstein, A.E. *Europ J Pharmacol*, 349, pp. 205-210, 1998.

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Research Findings

Behavioral Research

Phencyclidine- and Diazepam-Like Discriminative Stimulus Effects of Inhalants in Mice

It has been shown that abused solvents, such as 1,1,1-trichloroethane (TCE) and toluene, share certain pharmacological properties with central nervous system depressants, such as alcohol and anesthetic vapors. Several vapors were tested for diazepam (DZ)- and phencyclidine (PCP)-like discriminative stimulus effects to further explore their pharmacological specificity. In DZ-trained mice, methoxyflurane fully substituted, and TCE produced partially substituted for PCP. In a test for substitution of fluorothyl and toluene for DZ, neither produced appreciable DZ-lever responding at any concentration tested. On the other hand, toluene produced concentration- related partial substitution for PCP. Methoxyflurane, TCE, and fluorothyl produced no substitution for PCP. The substitution of some of these vapors for DZ or PCP suggests that, like ethanol, the discriminative stimulus effects of abused solvents partially overlap those of N-methyl-D- aspartate antagonists as well as those of gamma amino butyric acid agonists. Bowen, S.E., Wiley, J.L., Jones, H.E., and Balster, R.L. *Exp. Clin. Psychopharmacology*, pp. 28-37, 1999.

Naltrexone Pretreatment Decreases the Reinforcing Effectiveness of Ethanol and Saccharin but not PCP or Food in Rhesus Monkeys

Investigators at the University of Minnesota Medical School asked whether naltrexone's effect on reducing ethanol consumption results from selective changes in the reinforcing effectiveness of drug or non-drug reinforcers. Ethanol-maintained responding under progressive-ratio (PR) schedules was attenuated in a dose-dependent fashion by 0.3 and 1.0 mg/kg doses of naltrexone, and saccharin-maintained responding was also decreased at the 1.0 mg/kg dose. Additionally, after 5 days of naltrexone pretreatment, ethanol (8% w/v) - and saccharin-maintained responding immediately returned to or exceeded baseline levels, suggesting the development of tolerance. However, food- and PCP (0.25 mg/ml)-maintained responding and intake were not significantly affected by any of the naltrexone doses examined. This suggests that these reinforcers: 1) are not sensitive to naltrexone antagonism at the doses examined, 2) are mediated by non-opioid reinforcement mechanisms, and/or 3) have less intrinsic palatability. Rodefer, J.S., Campbell, U.C., Cosgrove, K.P., and Carroll, M.E. *Psychopharmacology*, 141, pp. 436-446, 1999.

Antinociceptive Effects of Cocaine in Rhesus Monkeys

Investigators at McLean Hospital/Harvard Medical School examined the antinociceptive effects of (-)cocaine, (+)cocaine, and cocaine methiodide alone and in combination with the mu-opioid agonist morphine in rhesus monkeys. Tail-withdrawal latencies from various warm water tail exposure durations (20-s maximum) were

determined. (-)Cocaine (0.032-1.8 mg/kg, s.c.) produced dose-dependent antinociceptive effects and enhanced the antinociceptive effects of morphine. Neither (+)cocaine nor cocaine methiodide (0.1-10 mg/kg, s.c.) produced antinociception or altered the effects of morphine. Pretreatment with the serotonin receptor antagonist mianserin (0.1 - 4.32 mg/kg, intra-muscularly (i.m.)) produced dose-dependent rightward shifts in the dose-effect curve for (-)cocaine alone, and attenuated its induced enhancement of the antinociceptive effects of morphine. However, mianserin (0.32 mg/kg, i.m.) did not alter the antinociceptive effects of morphine alone. These results suggest that in rhesus monkeys, the effects of cocaine on nociception may be stereoselective and centrally mediated. These findings further suggest that the antinociceptive effects of cocaine in primates may be mediated at least in part by cocaine's effects on serotonergic systems. Gatch, M.B., Negus, S.S., Mello, N.K. *Pharmacol. Biochem. Behav.*, 62, pp. 291-297, 1999.

Blocking Smoking Satisfaction With the Peripheral Nicotinic Antagonist Trimethaphan

Jed Rose and his colleagues at Duke University Medical Center investigated the role of peripheral nicotinic receptors in mediating the rewarding effects of cigarette smoking. Cigarette smokers rated cigarettes after intravenous infusion of the short-acting peripheral nicotinic receptor antagonist trimethaphan. Cigarette conditions included subjects' usual brand of cigarette, denicotinized tobacco cigarettes, and nicotine-injected cigarettes with the same tar delivery as denicotinized cigarettes but with an enhanced nicotine delivery equal to that of subjects' usual brands. (The latter cigarettes were rated as extremely harsh due to the high nicotine/tar ratio.) Compared with placebo, trimethaphan significantly attenuated the airway sensations associated with nicotine, and reduced satisfaction of the favored cigarette brand to the level of the other two cigarettes. These findings suggest that nicotinic receptors on peripheral nerve endings in the respiratory tract modulate smoking satisfaction and may be important in the maintenance of cigarette addiction. Rose, J.E., Westman, E.C., Behm, F.M., Johnson, M.P., Goldberg, J.S. *Pharmacol Biochem Behav.*, 62, pp. 165-172, 1999.

Smoked Cocaine Self-Administration in Females and Voucher Incentives for Abstinence

Researchers at New York State Psychiatric Institute and the College of Physicians and Surgeons of Columbia University previously developed and reported on a laboratory model of "binge use" of cocaine that permitted characterization of behavior during the binge and during withdrawal from the binge. These researchers have now attempted to extend their model to a sample of high-use female cocaine abusers. Because of logistical difficulties associated with recruiting females for extended inpatient studies, the investigators used a modified protocol in which the withdrawal phase was conducted on an outpatient basis using a voucher procedure to facilitate abstinence so that withdrawal effects could be assessed. In the initial inpatient 4 to 5-day "binge" phase, ten non-treatment seeking females were permitted to smoke up to 6 doses of 50 mg cocaine base in two daily "binge" sessions for two consecutive days. Cocaine's subjective and cardiovascular effects were consistent with those previously reported in males, with the exceptions of a within-binge decrease in cocaine craving and a within-binge increase in tiredness among females. In the subsequent 2-week out-patient abstinent period, urine samples and questionnaire responses were collected daily and subjects received merchandise vouchers each time their urine sample contained less cocaine metabolite than the prior sample and was negative for all other drugs tested. During the outpatient withdrawal phase, although session attendance was excellent (98%), because only 56% of the urines indicated no new cocaine use, cocaine withdrawal effects could not be assessed. Nevertheless, achievement of 56% daily abstinence in a group of non-treatment seeking, high-use cocaine abusers serendipitously points to the utility of using voucher incentives in this population. Smoked Cocaine Self-Administration in Females and Voucher Incentives for Abstinence. Evans, S.M., Levin, F.R, Fischman, M.W., and Foltin, R.W. *Journal of Substance Abuse*, 10, pp. 143-162, 1998.

Male Rats Exhibit Greater Morphine Tolerance and Dependence Than Female Rats

Several rodent studies have shown that morphine's antinociceptive effect is greater for males than females. Dr. Rebecca Craft and colleagues have now reported sex differences in tolerance to morphine's antinociceptive effect. In the first experiment, whereas acute single doses of either 3.0, 5.6, or 10 mg/kg morphine produced significantly greater hotplate and tail withdrawal antinociception in males than females, delivery of all three doses spaced one week apart ("repeated dosing") did not produce sex differences; however, in males, morphine's antinociceptive effect was greater under acute dosing than under repeated dosing, whereas in females the effect was the same under the two procedures. In Experiment 2, in which morphine was delivered chronically twice daily, males exhibited significantly greater tolerance to morphine's antinociceptive effect than females and they exhibited greater recovery. During this experiment, 7 of 31 males, but none of the 29 females, died of respiratory depression. Morphine produced

a decrease in the number of proestrus and estrus days and an increase in diestrus days. In Experiment 3, when morphine withdrawal was precipitated by naloxone, withdrawal scores were significantly greater for males than females with the greatest sex difference occurring in number of "wet-dog shakes." Craft, R.M., Stratmann, J.A., Bartok, T.I., and King, S.J. *Psychopharmacology*, 143, pp. 1-7, 1999.

Cue-Induced "Relapse" and "Priming" of Drug-Seeking Behavior: Dopaminergic Substrates in the Amygdala

The return of responding for drug during extinction, i.e. after terminating drug availability, has been suggested as a model of relapse. When the resurgence of responding is prompted by administering the previously self-administered drug, such as cocaine, this is known as "priming". Recent studies suggest that dopamine (DA) transmitter dynamics in the amygdala may play a role in incentive motivational processes that direct drug-seeking behavior during extinction. Dr. Janet Neisewander and colleagues at Arizona State University recently monitored extracellular DA in the amygdala during extinction and cocaine-priming. Different groups of rats were withdrawn for between one day and one month following two weeks of cocaine self-administration. Returning the animals to the self-administration chamber resulted in significant lever presses on the manipulandum that previously delivered cocaine. This drug-seeking behavior was accompanied by significant elevations of amygdaloid DA only in the one month withdrawal group. When i.p. cocaine was given to "prime" drug-seeking responses, rats under all withdrawal durations showed significant increases of DA overflow and also pressed the response lever that previously delivered drug infusions. However, animals from the one month withdrawal group had significantly greater increases in both the neurochemical and behavioral measures than did those in the other withdrawal conditions. These observations suggest that DA in the amygdaloid nuclei may be important in the neurochemical mechanisms underlying the "priming" effect. Furthermore, it appears that priming may be enhanced at more protracted post-withdrawal intervals. Tran-Nguyen, L.T.L., Fuchs, R.A., Coffey, G.P., Baker, D.A., O'Dell, L.E., and Neisewander, J.L. *Neuropsychopharmacology*, 19, pp. 48-59, 1999.

Motivational and Experiential Factors in the Development of Psychostimulant Tolerance

Dr. David Wolgin at Florida Atlantic University has been studying contingencies that modulate the development of tolerance to psychostimulants such as amphetamine. This approach emphasizes motivational and cognitive factors in drug-induced neuroadaptations that manifest as behavioral tolerance or sensitization. He has previously reported that animals will suppress stereotypical motor behaviors that interfere with the ingestion of a sweet milk solution and has proposed that tolerance to amphetamine's hypophagic effects can be attributed to this behavioral modulation. In a recent publication, he demonstrates that even animals with extremely high frequencies of amphetamine-induced stereotypy are capable of inhibiting this motor disruption and developing tolerance to amphetamine-induced hypophagia. In this study, Dr. Wolgin administered a chronic regimen of 5.0 mg/kg d-amphetamine to rats and observed enhanced stereotypical responding produced by this dose over the repeated administration. He then repeatedly administered 2.0 mg/kg d-amphetamine while animals consumed sweetened milk from a drinking spout. He found that the sensitized stereotypical responses did not interfere with the development of tolerance. This finding suggests that, given an appropriate incentive, rats can actively learn to suppress the expression of psychostimulant sensitization. If sensitization is an important process in the escalation of drug-seeking behavior, then the motivation to acquire non-drug rewards may contribute to the suppression of sensitization. Hughes, K.M., Popi, L., and Wolgin, D.L. *Psychopharmacology*, 140, pp. 445-449, 1999.

Abstinence Syndrome After Cessation from Smoked Marijuana in Humans

Precipitated withdrawal from delta9-tetrahydrocannabinol (THC), the major psychoactive component in marijuana, has been demonstrated in rats and there are clinical reports that abusers attempting to abstain from smoking marijuana experience a withdrawal syndrome. Investigators at the New York State Psychiatric Institute are the first to demonstrate physiological withdrawal symptoms accompanying the cessation of smoked marijuana in the laboratory. Twelve habitual marijuana smokers in a residential laboratory smoked marijuana cigarettes containing 1.8 or 3.1 percent THC. These investigators found, in comparison to placebo cigarettes, that ratings of anxiety were significantly increased during abstinence from 1.8 percent THC, and that ratings of stomach pain and irritability were increased during abstinence from 1.8 percent and 3.1 percent THC, respectively. There were also significant *decreases* in reports of being talkative, energetic and social during these abstinence periods as compared to baseline. Subjects were less accurate in tracking moving targets on a divided attention task following withdrawal. These data suggest that continued marijuana abuse may be driven by avoidance of negative abstinence symptoms, in addition to the

direct reinforcing effects of the drug itself. Haney, M., Ward, A.S., Comer, S.D., Foltin, R.W., and Fischman, M.W. *Psychopharmacology*, 141, pp. 395-404, 1999.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****May, 1999**

Research Findings

Clinical and Services Research

Moderate Versus High Dose Methadone in the Treatment of Opioid Dependence: A Randomized Trial

Drs. Strain, Bigelow, Liebson and Stitzer of the Department of Psychiatry and Behavioral Sciences at the Johns Hopkins University School of Medicine, assessed the relative efficacy of moderate (40-50 mg.) versus high (80-100 mg) oral dose methadone in the treatment of opioid dependence. Results of a 40-week, randomized, double-blind clinical trial, conducted in an outpatient substance abuse treatment research clinic, suggest the high-dose group (N=95) experienced significantly greater decreases in illicit opioid use than did the medium-dose group (N=97), although patients from both groups showed a decrease in illicit opioid use during methadone maintenance and detoxification. Strain, E.C., Bigelow, G.E., Stitzer, M.L. *Journal of the American Medical Association*, 281(11), pp. 1000-1005, 1999.

History of Alcohol or Drug Problems, Current Use of Alcohol or Marijuana, and Success in Quitting Smoking

Dr. Humfleet and colleagues at the University of San Francisco examined the relationship of alcohol and drug treatment history and current alcohol and marijuana consumption with success in smoking cessation treatment in a smoking clinic population. No significant differences in abstinence rates were found based on history of alcohol/drug problem or treatment. Both alcohol use at baseline and any alcohol use during treatment predicted smoking at all follow-up points. Alcohol users had significantly lower quit rates than did participants reporting no use. Neither use of marijuana at baseline nor during treatment predicted outcome. Past alcohol and drug problems do not appear to predict treatment outcome, however, even low to moderate levels of alcohol consumption during smoking cessation may decrease treatment success. Humfleet, G., Munoz, R., Sees, K., Reus, V., and Hall, S. *Addictive Behaviors*, 24, pp. 149-154, 1999.

Abstinence-Based Vouchers Increase Marijuana Abstinence During Outpatient Treatment for Marijuana Dependence

Dr. Alan Budney and colleagues at the University of Vermont tested the efficacy of an abstinence-based voucher program with persons seeking treatment for marijuana dependence. Participants (N=60) were randomly assigned to one of three treatments: brief motivational therapy (M), brief therapy combined with behavioral coping-skills therapy (MBT), or a combination of the brief therapy, the coping-skills therapy and voucher program (MBTV). The voucher

program involved providing monetary-based incentives contingent on subjects' submitting urine specimens free of cannabinoids. A significantly greater number of subjects in the MBTV group compared with the MBT or M groups were abstinent at the end of the 14-week treatment (35% vs. 10% vs. 5%, respectively). This is the first trial to show that an abstinence-based voucher program can improve marijuana abstinence rates in the treatment of marijuana dependence. Paper presented at the 1998 conference of the American Public Health Association, Washington, D.C. and the 1998 conference of the College on Problems of Drug Dependence, Scottsdale, AZ.

Manipulation of Cigarette Craving through Rapid Smoking: Efficacy and Effects on Smoking Behavior

Drs. Stitzer and Houtsmuller at Johns Hopkins University attempted to 1) identify interventions that can reliably influence cigarette cravings, and 2) assess the relationship between cigarette craving and smoking behavior. The effects of aversive rapid smoking on self-reported craving and subsequent smoking behavior were compared to effects of self-paced smoking or no smoking. Subjects (N=14) engaged in a rapid, self-paced or no smoking procedure at the start of three separate sessions. Craving levels, measured repeatedly during the next 3 hours of no smoking, were significantly lower after rapid smoking than after either self-paced or no smoking. Measures of subsequent smoking behavior (latency to first cigarette; number of cigarettes, number of puffs) did not differ systematically across conditions. Thus craving was reliably suppressed by aversive rapid smoking, but craving scores did not predict actual smoking behavior. Houtsmuller, E.J., Stitzer, M.L. *Psychopharmacology*, 142, pp. 149-157, 1999.

Contingent Reinforcement Sustains Post-detoxification Abstinence From Multiple Drugs: A Preliminary Study with Methadone Patients

In a study examining the efficacy of a urinalysis-based contingency management program for preventing relapse to abused drugs following brief residential detoxification, 14 chronic benzodiazepine abusing methadone-maintained patients enrolled in a 7-day residential detox were randomly assigned to receive either Contingency Management or Standard Care upon return to outpatient methadone treatment. The contingency management condition was either a take-home dose of methadone or a \$25 voucher (patient choice) for each urine that was free of opiates, cocaine, and benzodiazepines. Preliminary data analysis showed that the Contingency Management patients submitted more drug-free urine samples during the behavioral intervention compared to pre-detoxification, whereas no significant changes were observed from pre-to post-detoxification in the Standard Care patients. Abstinence-based contingency management may be a promising strategy for preventing relapse to multiple drugs of abuse in a subpopulation of methadone maintenance patients when abstinence has been initiated through brief residential detoxification. Chutuape, M., Silverman, K., and Stitzer, M., *Drug and Alcohol Dependence*, 54, pp. 69-81, 1999.

Disulfiram Effects on Acute Cocaine Administration

This randomized, double-blind, placebo-controlled within subjects study was conducted (in 7 subjects meeting DSM-IV criteria for cocaine dependence and alcohol abuse) to determine whether disulfiram (250 or 500mg/day or placebo) alters responses to acute intranasal cocaine (1 or 2mg/kg , placebo) administration. Effects of disulfiram on cocaine pharmacokinetics, physiological, and behavioral responses were determined. Disulfiram treatment increased plasma cocaine concentrations three to six times and significantly increased cocaine-associated cardiovascular responses, but did not alter the behavioral responses to cocaine. This study provides evidence of a significant interaction between cocaine and disulfiram which should be considered in the decision regarding disulfiram treatment in cocaine dependent patients. McCance-Katz, E., Kosten, T., and Jatlow, P. *Drug and Alcohol Dependence* (52), pp. 27-39, 1998.

A Nicotine Antagonist, Mecamylamine, Reduces Cue-Induced Craving in Cocaine-Dependent Subjects

Dr. Malcolm S. Reid and colleagues at the New York Veterans Affairs Medical Center and at the San Francisco Veterans Affairs Medical Center reported that mecamylamine, a nicotine antagonist, attenuated cue-induced cocaine craving. Twenty-three cocaine-dependent subjects who were also cigarette smokers were randomly assigned to either mecamylamine or placebo in a single-dose, placebo controlled, cross-over, double blind study. Various measures of

craving and anxiety were recorded before and during cocaine cues. While all subjects reported an increase in craving, anxiety, skin conductance and skin temperature in response to cocaine cues, the cue-induced increase in cocaine craving was reduced, while skin conductance and skin temperature were unaffected for subjects on mecamlamine. This suggests that mecamlamine, in reducing cue-induced cocaine craving, may have potential as a cocaine pharmacotherapy. Reid, M.S., Mickalian, J.D., Delucci, K.L. and Berger, K.S. A Nicotine Antagonist, Mecamlamine, Reduces Cue-Induced Craving in Cocaine-Dependent Subjects. *Neuropsychopharmacology*, 20, pp. 297-307, 1999.

Concurrent Use of Cocaine and Alcohol is More Potent and Potentially More Toxic Than the Use of Either Alone

In this double-blind, randomized within subjects study, 8 volunteers meeting DSM-IV criteria for cocaine dependence and alcohol abuse participated in 3 drug administration sessions: four doses of intranasal cocaine (1mg/kg every 30 min.) with oral alcohol (1 g/kg) administered following the initial cocaine dose and a second dose (120mg/kg) at 60 minutes calculated to maintain plasma alcohol concentration at approximately 100mg/dL during the cocaine administration; four doses of cocaine/placebo alcohol; four doses of cocaine placebo/alcohol. Pharmacokinetic, physiological, and behavioral effects were followed over 8 hours. Simultaneous administration of cocaine and alcohol produced greater euphoria and increased perception of well-being relative to cocaine alone. In addition, heart rate significantly increased following the cocaine and alcohol administration relative to either drug alone. The enhanced psychological effects may encourage ingestion of larger amounts of these substances over time placing users at increased risk for greater toxicity than with either drug alone. McCance-Katz, E., Kosten, T., and Jatlow, P., *Biological Psychiatry*, (44) pp. 250-259, 1998.

Research versus "Real World" Patients: Representativeness of Participants in Clinical Trials of Treatments for Cocaine Dependence

To assess the representativeness of subjects participating in clinical trials, 243 research subjects participating in clinical trials of treatments for cocaine dependence were compared to a sub-sample of 213 individuals being treated for cocaine dependence in outpatient clinical settings from a large national database. The findings from this study suggest that research patients participating in clinical trials are similar to, if not more severe than, individuals with cocaine problems in regular clinical and community-based treatment settings. Carroll, K., Nich, C., McLellan, T., McKay, J., and Rounsaville, B. *Drug and Alcohol Dependence* (54), pp. 171-177, 1999.

Persistence of Viremia and the Importance of Long-Term Follow-up After Acute Hepatitis C Infection

The purpose of this investigation was to prospectively characterize acute hepatitis C virus (HCV) infections and to evaluate the hypothesis the outcome is affected by identifiable clinical or viral factors. In a study of 142 IDUs who were HCV antibody negative in 1988 and who were followed semi-annually through 1996, HCV seroconversion was observed in 43 (30%). HCV RNA was detected and quantified in a median of 10 specimens per participant and showed two distinct patterns of viremia: viral clearance was noted in 6 (14%) and viral persistence was observed in 37 (86%) participants. Subjects with viral clearance were more likely to be white ($p=.004$), have jaundice ($p=.03$), and have lower peak viral titer ($p=.003$). However, the outcome for a given person could not be predicted by clinical features, RNA level, or HCV subtype. No acute infections were recognized by health care workers. At the time of seroconversion, HCV RNA was detectable in 81% of participants, and recombinant immunoblot assay was positive in 85%. The authors conclude that approximately 85% of those with acute hepatitis C develop persistent viremia; however, acute infections are uncommonly recognized clinically, underscoring the importance of screening those at risk. Long-term follow-up, but no single lab test, is necessary to ascertain the outcome and in some cases make the diagnosis of acute HCV infection. Villano, S.A., Vlahov, D., Nelson, K.E., Cohn, S., and Thomas, D.L. Persistence of Viremia and the Importance of Long-Term Follow-Up after Acute Hepatitis C Infection. *Hepatology*, 29, pp. 908-914, 1999.

Ambient Temperature and Mortality From Unintentional Cocaine Overdose

The Cornell University Medical College researchers, Marzuk, Tardiff and colleagues conducted a retrospective medical examiner surveillance study to assess the association of hot weather with mortality from unintentional cocaine

overdose. All cases of fatal unintentional drug overdoses in New York City from 1990 through 1995 were identified through manual review of all medical files at the Office of Chief Medical Examiner of New York. The study population consisted of all fatal unintentional cocaine overdoses from 1993 through 1995 (n=2008). The contemporaneous comparison groups included fatal unintentional opiate overdoses (n=793), all other fatal unintentional overdoses (n=85) and a subset of homicides (n=4638) and fatalities from motor vehicle crashes (n=815). A temperature threshold of 31.1°C (88°F) was identified, above which the mean daily number of fatal cocaine overdoses increased steadily. On days with a maximum daily temperature of 31.1°C or higher ("hot days"), the mean daily number of cocaine overdose deaths was 2.34 (SD=1.68), which was 33% higher than the mean on days with a maximum temperature of <31.1°C (mean=1.76 [SD=1.37], p<0.001). In contrast, the opiate overdose deaths/day was 0.81 on hot days and 0.71 on other days. The proportions with a positive cocaine toxicology among homicides and traffic fatalities did not differ significantly on hot days from those on other days. The investigators concluded that high ambient temperature is associated with a significant increase in mortality from cocaine overdose. The increase was not explained by changes in cocaine use among the general population. They stated that although cocaine use is dangerous on all days, it appears to be even more dangerous on hot days. Marzuk, P., Tardiff, K., Leon, A., Hirsch, C.S., Portera, L., Iqbal, M.I., Nock, M.K., and Hartwell, N. Ambient Temperature and Mortality From Unintentional Cocaine Overdose. JAMA, 279, pp. 1795-1800, 1998.

Hallucinogens and Residual Neuropsychological Toxicity

Halperin and Pope searched the Medline database between 1964 and 1998 and reviewed the published articles on hallucinogens (LSD, Mescaline, Psilocybin, Psilocin, DMT, and MDMA). Of the several hundred citations in the literature, a total of 42 investigations were found where neuropsychological tests had been administered to the subjects. After applying various inclusion and exclusion criteria, only nine qualifying studies were found where the subjects were administered the appropriate neuropsychological tests to assess the residual, but not the acute effects of hallucinogens. The authors conclude that interpretation of the studies was limited by various confounding variables, such as subjects' premorbid cognitive and personality function and prior use of other substances. The literature tentatively suggests that there are few, if any, long-term neuropsychological deficits attributable to hallucinogen use. To better resolve this issue, it will be important to study larger samples of chronic, frequent hallucinogen users who have not often used other types of drugs Halperin, J. and Pope, H. Do Hallucinogens Cause Residual Neuropsychological Toxicity? Drug and Alcohol Dependence, 53, pp. 247-256, 1999.

Dynorphin Lowers Dopaminergic Tone Acting through Opioid Receptor Mechanisms

Dr. Mary Jeanne Kreek and associates demonstrated that administration of dynorphin increased prolactin levels suggesting a reduction of dopaminergic tone that modulates that system. It was further demonstrated that this action likely occurred through *kappa* and possibly *mu* opioid receptors. Furthermore, females were more responsive than males. These results suggest that a dynorphin-like compound might be useful in managing cocaine addiction. (Kreek, M.J., Schluger, J., Borg, L., Bunduz, M., and Ho, A. The Journal of Pharmacology and Experimental Therapeutics, 288(1), pp. 260-269, 1999) Dynorphin was also administered as a possible treatment for opioid withdrawal. Opiate-dependent subjects who had been stabilized on morphine received a single dose of dynorphin A(1-13) with positive results. There was some reduction in symptomatology at the higher doses (500 micrograms), but these were not dose-dependent. Specker, S., Wananukul, W., Hatsukami, D., Nolin, K., Hooke, L., Kreek, M.J., and Pentel, P.R. Psychopharmacology, 137, pp. 326-332, 1998.

Regional Brain Metabolic Activation During Craving

Dr. Nora Volkow and colleagues at the Brookhaven National Laboratory investigated cerebral circuits involved in cue-elicited craving. Thirteen cocaine abusers were scanned using positron emission tomography (PET). Craving was induced during an interactive interview about neutral versus cocaine themes. In addition to the PET scans, behavioral and cardiovascular responses were recorded. During the cocaine theme interview, subjects reported higher self reports for cocaine craving and had higher heart rates, systolic and diastolic blood pressures than during the neutral theme interview. Metabolic (both absolute and relative) values were higher during the cocaine theme than the neutral theme in the orbitofrontal and left insular cortex, and relative values were higher in the cerebellum. Relative metabolic values in the right insular region were correlated significantly with self reports of cocaine craving. The activation during the cocaine theme of the temporal insula, a brain region implicated in autonomic control, and of the orbitofrontal cortex, a brain region involved in expectancy and reinforcing salience of stimuli, support their involvement with craving in chronic cocaine users. Wang, J.G., Volkow, N.D., Fowler, J.S., Cervany, P., Hitzemann,

R.J., Pappas, N.R., Wong, C.T., and Felder, C. Regional Brain Metabolic Activation During Craving Elicited by Recall of Previous Drug Experiences. *Life Sci*, 64(9), pp. 775-784, 1999.

Limbic Activation During Cue-Induced Cocaine Craving

Dr. Anna Rose Childress and colleagues at the University of Pennsylvania School of Medicine tested whether limbic activation occurs during cue-induced craving in humans. Using positron emission tomography (PET), relative regional cerebral blood flow (CBF) was measured in limbic and comparison brain regions in detoxified and cocaine-naïve subjects during exposure to cocaine-related and neutral, nondrug-related videos. Results revealed that during the cocaine video, the cocaine users experienced craving and showed a pattern of CBF increases in the amygdala and anterior cingulate, with concomitant decreases in the basal ganglia relative to the responses to the nondrug video. Drug-naïve subjects did not show this pattern of CBF change, and the two groups did not differ in their responses in the comparison regions. It was concluded that limbic activation is one component of cue-induced cocaine craving. Childress, A.R., Mozley, D.P., McElgin, W., Fitzgerald, J., Reivich, M., and O'Brien, C.P. *Limbic Activation During Cue-Induced Cocaine Craving*. *Am. J. Psychiatry*, 156, pp. 11-18, 1999.

How Are Women Who Enter Substance Abuse Treatment Different than Men?: A Gender Comparison from the Drug Abuse Treatment Outcome Study

Gender differences at admission to treatment were examined in a large sample (N=10,010) of men and women entering four major substance abuse treatment modalities in the Drug Abuse Treatment Outcome Study (DATOS). Women were younger and less educated than men and had been employed less. Although some drug use patterns were similar, men reported more alcohol use while women reported greater daily use of cocaine. Women reported more problems related to health and mental health. In addition, women reported higher levels of past and current physical and sexual abuse. Both men and women who had custody of children showed concern that drug treatment might affect their custody, but most other issues related to children are still primarily women's issues. Wechsberg, W.M., Craddock, S.G., & Hubbard, R.L. *Drugs and Society*, 13(1/2), pp. 97-115, 1998.

Women in Residential Drug Treatment: Differences by Program Type and Pregnancy Attitudes

This study compared the characteristics of 4,117 women treated in publicly-funded residential drug treatment programs in Los Angeles County between 1987-1994 by pregnancy status and program gender composition, i.e., women-only and mixed gender programs. A logistic regression analysis determined the predictors of program completion. Patients in women-only programs were more likely than women in mixed-gender programs to be pregnant, homeless, on probation, to use methamphetamines, to use alcohol, and to have prior drug treatment. Pregnant women were younger, more likely to be homeless, had fewer years of drug use, were more often referred to treatment by other services providers, and were less likely to have injected drugs or have prior drug treatment than non-pregnant women. Patients in women-only programs spent more time in treatment and were over twice as likely to complete treatment as women in mixed gender programs. Grella, C.E., *Journal of Health Care for the Poor and Underserved*, 10(2), May 1999.

Substance Use, Mental Disorders, Abuse and Crime: Gender Comparisons Among a National Sample of Adolescent Drug Treatment Clients

This paper describes important gender comparisons in drug and alcohol use, illegal activity, physical and sexual abuse, and mental health problems among a large sample of adolescents (N=3,382) who were treated from 1993 to 1995 in adolescent-oriented drug programs that participated in the Drug Abuse Treatment Outcome Study of Adolescents. Most of the adolescents reported regular use of marijuana and alcohol. Males had higher rates of illegal activity and involvement with the juvenile justice system. Females reported more sexual abuse, while males reported more physical abuse. Males and females had equal rates of conduct disorder and attention deficit hyperactivity disorder. Rounds-Bryant, J. L., Kristiansen, P.L., Fairbank, J.A., & Hubbard, R.L. *Journal of Child & Adolescent Substance Abuse*, 7(4), pp. 19-34, 1998.

Parity for Mental Health and Substance Abuse Care under Managed Care

Most health care plans restrict benefits for behavioral treatment, especially mental health and substance abuse care, to limit their financial risk of paying for costly long-term illnesses. These benefit restrictions have been criticized as unfair and unnecessary by many who seek parity between medical care and behavioral health care coverage. However, benefit restrictions have become less important in allocating health care resources and controlling costs due to the impact of managed care. The implication of managed care for policies aimed at achieving parity in insurance coverage was examined using a theoretical approach to examine adverse selection, moral hazard (over-utilization of benefits), and other insurance issues. The researchers found that due to the control of managed care on cost and utilization, parity in benefit design no longer implies equal access to or quality of mental health and substance abuse care. Similarly, parity has less value in avoiding adverse selection, the enrollment of high-cost members in a health plan with a comparatively lenient benefit structure. Frank, R.G. and McGuire, T.G. *Journal of Mental Health Policy and Economics*, 1(4), pp. 153-159, 1998.

Mental Health and Substance Abuse Parity: A Case Study of Ohio's State Employee Program

In the United States, insurance benefits for treating alcohol, drug abuse and mental health (ADM) problems have been much more limited than medical care benefits. This study documents the experience of the State of Ohio with adopting full parity for ADM care for its state employee program under managed care. In contrast to the emerging inflation anxiety regarding overall healthcare costs, managed care can provide long-run cost containment for ADM care when patient copayments are reduced and coverage limits are lifted. This may differentiate ADM care from medical care and reasons may include the state of management techniques (much higher technology utilization in medical care) and demographic factors (medical, but not behavioral health costs increase as the population ages). This study indicates that a parity level benefit for ADM care is affordable under managed care. Sturm, R., Goldman, W. and McCullugh, J. *Journal of Mental Health Policy and Economics*, 1(4), pp. 129-134, 1998.

Legal Pressure and Treatment Retention in a National Sample of Long-Term Residential Programs

This study examined the association between legal pressure and treatment retention in a national sample of 2,605 clients admitted to 18 long-term facilities that participated in the Drug Abuse Treatment Outcome Study (DATOS). Hierarchical linear models were used to assess the relationship of background factors and legal pressure with treatment participation for 90 days or longer. Two thirds of the sample entered residential treatment with moderate to high pressure from legal authorities, and they were significantly more likely than the low-pressure clients to stay 90 days or more. Moreover, the difference in retention between moderate-to-high and low-pressure clients was even greater in programs with proportionally larger caseloads under legal surveillance. The criminal justice system (CJS) can influence treatment participation and retention, and it appears essential for the CJS and treatment programs to maintain an open and constructive relationship to maximize their potential combined impact. Hiller, M.L., Knight, K., Broome, K.M., Simpson, D.D., *Criminal Justice and Behavior*, 25(4), pp. 463-481, 1998.

Effects of Readiness for Drug Abuse Treatment on Client Retention and Assessment of Process

This study examined client motivation as a predictor of retention and therapeutic engagement across the major types of treatment settings represented in the third national drug abuse treatment outcome study (DATOS) conducted in the United States. Sequential admissions during 1991-1993 to 37 programs provided representative samples of community-based treatment populations. Based on this naturalistic non-experimental evaluation design, hierarchical linear model (HLM) analysis for nested data was used to control for systematic variations in retention rates and client attributes among program within modalities. The data were collected from long-term residential (LTR), outpatient methadone (OMT), and outpatient drug free (ODF) programs located in 11 large cities. A total of 2265 clients in 18 LTR, 981 clients in 13 OMT and 1, 791 clients in 16 ODF programs were studied. Pre-treatment variables included problem recognition and treatment readiness (two stages of motivation), sociodemographic indicators, drug use history and dependence, criminality, co-morbid psychiatric diagnosis and previous treatment. Retention and engagement (based on ratings of client and counselor relationships) served as outcome criteria. Pre-treatment motivation was related to retention in all three modalities, and the treatment readiness scale was the strongest predictor in LTR and OMT. Higher treatment readiness also was significantly related to early therapeutic engagement in each modality. Indicators of intrinsic motivation-especially readiness for treatment-were not only significant predictors of engagement and retention, but were more important than sociodemographic, drug use, and other background variables. Joe, G.W., Simpson, D.D., Broome, K.M., *Addiction*, 93(8), pp. 1177-1190, 1998.

Antisocial Tendency Among Drug-Addicted Adults: Potential Long-Term Effects of Parental Absence, Support, and Conflict During Childhood

This study examined the relationship between perceptions of parent-child relations in the family of origin and antisocial tendency in a sample of drug-addicted adults. Data included retrospective accounts of childhood family factors, adolescent antisocial tendency and self-reported hostility and risk-taking prior to treatment entry. A developmental model was tested that included adolescent antisocial tendency as a mediator of the relationship between childhood parenting factors and adulthood antisocial tendency. The effects of parental support and conflict were found to operate primarily through adolescent measures of antisocial tendency. Specifically, lower levels of parental support and higher levels of conflict with parents predicted greater adolescent antisocial tendency, which in turn predicted more hostility and risk-taking in adulthood. Thus, parental support appears to serve as a buffer against deviant behavior and drug use. Knight, D.K., Broome, K.M., Cross, D.R., Simpson, D.D., *American Journal of Drug and Alcohol Abuse*, 24(3), pp. 361-375, 1998.

Residential Drug Abuse Treatment for Probationers: Use of Node-Link Mapping to Enhance Participation and Progress

Node-link mapping, a tool to improve communication between patients and counselors using visual representation of the relationships between behaviors, was used to enhance substance-abuse treatment in a 4-month residential criminal justice program. Twelve communities of 30 to 35 probationers ("residents") were randomly assigned to either mapping-enhanced or standard counseling. During group sessions, counselors and residents in the mapping communities collaborated to develop node-link maps representing critical behavioral issues. Counselors in standard communities used their own methods. Treatment motivation (i.e., desire for help) was assessed at intake and was used to categorize residents into three levels. Treatment involvement was measured at the middle and at the end of the program. Residents, as well as their counselors, rated those in mapping communities as participating more in group sessions than those in standard communities. Mapping residents also reported better personal progress toward treatment goals, more positive affective responses to treatment, and greater treatment engagement. Residents with higher motivation at intake had higher treatment involvement scores regardless of type of counseling received. Piter, U., Dansereau, D.F., Newbern, D. and Simpson, D.D. *Journal of Substance Abuse Treatment*, 15(6), pp. 535-543, 1998.

A Comparison of Two Methods for Estimating the Costs of Drug Abuse Treatment

A consistent method has not been used to estimate the costs of providing substance abuse treatment. Most previous studies used direct "out-of-pocket" expenditures as an approximation of the total value of treatment services. The risk of this method is to ignore the value of resources that are partially subsidized or used without cost to the program. This paper compares the accounting and economic approach utilizing two outpatient methadone clinics and two residential treatment programs. The study finds that economic costs are from 4 to 15 percent higher than accounting costs. Dunlap, L.J. and French, M.T. *Journal of Maintenance in the Addictions*, 1(3), pp. 29-44, 1998.

The Development and Validation of a Simpatia Scale for Hispanics Entering Drug Treatment

A 17-item simpatia scale was developed for use with Hispanic substance abusers using confirmatory factor analytic techniques in a sample of 144 daily opioid users. The overall scale had good internal consistency and demonstrated convergent and discriminant validity. The simpatia scale was constructed to examine social attributes reflecting agreeableness, respect of others, and politeness. The Agreeableness subscale addressed issues related to agreeing with others, similarity of opinions between self and others, and if clients openly disagreed with others. The Respect subscale addressed issues related to saying good things about others, trusting others, and treating others with respect. The Politeness subscale addressed issues related to avoiding conflict with others, doing favors, and treating others as equals. A cross-validation study demonstrated that simpatia was positively related to social support, social conformity, treatment service satisfaction, and client rating of counselor skills, whereas it was negatively related to hostility. Griffith, J.D., Joe, G.W., Chatham, L.R., Simpson, D.D. *Hispanic Journal of Behavioral Sciences*, 20(4), pp. 468-482, 1998.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****May, 1999**

Research Findings

AIDS Research

Plasma Virus Load Evaluation in Relation to Disease Progression in HIV-Infected Children

Savita Pahwa and colleagues at North Shore University Hospital, Manhasset, New York, observed that high levels of HIV RNA (measured retrospectively by nucleic acid sequence-based amplification assay) in infancy is associated with increased mortality, although no correlation was observed between levels of cellular HIV DNA and plasma HIV RNA. Tetali, S., Bakshi, S., Than, S., Pahwa, S., Abrams, E., Romano, J., and Pahwa, S. G. Plasma Virus Load Evaluation in Relation to Disease Progression in HIV-Infected Children. *AIDS Res. Hum. Retroviruses*, 14(7), pp. 571-577, 1998.

Direct Comparison of Time to AIDS and Infectious Disease Death Between HIV Seroconverter IDUs in Italy and the U.S.: Results from the ALIVE and ISS Studies

The rate of HIV disease progression was compared in two cohorts: one a U.S. cohort of active polysubstance injectors (ALIVE) and the other an Italian cohort of predominantly opiate injectors (ISS). Data from the two cohorts were combined and the seroconversion date was estimated as the midpoint between the last negative and first positive HIV test. Time to AIDS or infectious disease death was calculated, adjusting for age at seroconversion, gender, and year of seroconversion. Of the 1003 IDUs, 226 progressed to AIDS and 146 died after AIDS diagnosis or from an infectious disease. Although the univariate analysis suggested possible differences for progression to AIDS or to infectious disease death between cohorts, multivariate analyses which adjusted for age showed no significant differences by cohort, gender, race, or time of seroconversion. The median time to AIDS for 25 year old persons in ALIVE was 12.3 years vs. 11.8 years in the ISS; for 35 year old persons the median time to AIDS 8.5 and 8.2 years, respectively. These estimates were similar to those for non-IDUs observed in the ISS and for homosexual men in a large U.S. cohort study. These results confirm the importance of accounting for age in considering the incubation period for HIV infection. Despite differences in drug use characteristics, the similar median times to AIDS, for each age, between the two cohorts of IDUs and between the IDUs and the non-IDUs, suggest a negligible effect of active injection drug use on HIV progression. Pezzotti, P., Galai, N., Vlahov, D., Rezza, G., Lyles, C.M., and Astemborski, J. Direct Comparison of Time to AIDS and Infectious Disease Death between HIV Seroconverter IDUs in Italy and the U.S.: Results from the ALIVE and ISS Studies. *J Acquir Immune Defic Syndr Hum Retrovirol* 20, pp. 275-282, 1999.

HIV Among Trauma Patients in New York City

The Cornell University Medical College investigators, Tardiff and his colleagues conducted a descriptive survey to determine the HIV seroprevalence rates in relation to the demographic characteristics of victims, cause of death, and

toxicology findings in a sample of victims of violence and accidents who presented to emergency departments before death. The survey was conducted in 5 boroughs of New York City (population, 7.3 million). Persons 15 years of age and older injured by intentional violence or accidents (excluding drug overdoses, falls, and suicides) who presented to hospitals, died and were sent to the medical examiner were included. Plasma and sera were analyzed for HIV and cocaine and its metabolites. Logistic regression and other appropriate statistical tests analyzed the data. Among the 1,242 subjects in the sample, 90 (7.2%) had positive findings: male patients (8%) having higher rates of HIV than females (3.4%). Among the various age groups, HIV rates were 20.8%, 9.6% and 8.1% among patients 35-44, 45-54, and 25-34-year age groups, respectively. Further, HIV rates among victims of homicides, accidents, and motor vehicle crashes were 8.2%, 10.5%, and 4%, respectively. Patients with positive results for cocaine (16.3%) were more likely than those with negative results (5.8%) to be HIV positive. Logistic regression analyses found that only age and positive cocaine results, not sex race, were related to increased risk of HIV infection. The investigators concluded that the rate of HIV infection among victims of fatal trauma was significant, especially in those with evidence of cocaine use. The results further emphasize the need for use of universal precautions in the care of trauma patients. Tardiff, K., Marzuk, P., Leon, A.C., Hirsch, C.S., Portera, L., and Hartwell, N. Human Immunodeficiency Virus Among Trauma Patients in New York City. *Annals of Emergency Medicine*, 32, pp. 151-154, 1998.

Effects of Chronic Opioid Dependence and HIV-1 Infection on Pattern Shift Visual Evoked Potentials

Bauer (University of Connecticut) examined the effects of opioid dependence, alone and in combination with asymptomatic HIV-1 infection, on the transmission of visual information from the retina to occipital cortex via measurements of the pattern shift visual evoked potential (PSVEP). For this purpose, three groups of patients were evaluated, including patients characterized by: (1) a past history (2-4 months abstinent) of DSM-III-R opioid dependence (i.e., in partial remission); (2) a recent history (7 days abstinent) of opioid dependence with ongoing methadone maintenance; and (3) a recent history of opioid dependence, ongoing methadone maintenance, and asymptomatic HIV-1 infection. A group of healthy, non-drug-dependent volunteers was also evaluated. The data analysis revealed no PSVEP differences between patients with a past history of opioid dependence and healthy volunteers. There were also no PSVEP differences between methadone-maintained patients with or without HIV-1 infection. Collectively, however, the two methadone maintenance groups exhibited significant delays in the N75 and P100 components of the PSVEP relative to the other two groups. The delay in N75 latency was strongly correlated with self-reported years of heroin abuse, but not with years of cocaine, alcohol, or other drug abuse. The nonsignificant trend toward delayed N75 latencies among asymptomatic HIV-1 seropositive drug abusers is better explained by their greater exposure to the neurotoxic effects of heroin than by coincident HIV-1 infection. Bauer, L.O. Effects of Chronic Opioid Dependence and HIV-1 Infection on Pattern Shift Visual Evoked Potentials. *Drug and Alcohol Dependence*, 50, pp. 147-155, 1998.

Viable, Proliferating HIV-1 Recovered From Syringes in Excess of Four Weeks Later

Using a microculture assay to detect viable virus in volumes of blood typical of those commonly found inside used syringes, and modeling the worse-case scenario, researchers determined the duration of survival of HIV-1 in syringes typically used by injectors of illicit drugs. They recovered viable, proliferating HIV-1 from syringes that have been maintained at room temperature for periods in excess of four weeks. The percentage of syringes with viable virus varied with the volume of residual blood and the titer of HIV-1 in the blood. Syringes with detachable needles were found to harbor more blood between their plunger and base, indicating that they may be riskier for HIV transmission than syringes with needles that do not detach. The likelihood of encountering a potentially infectious syringe decreased with time but remained finite for an extended period. The researchers suggest that, in the absence of bleach, postinjection flushing with clean water may lessen chances of HIV transmission. Abdala, N., Stephens, P.C., Griffith, B.P., and Heimer, R. Survival of HIV-1 in Syringes. *J AIDS Hum Retroviol*, 20, pp. 73-80, 1999.

Researchers Examine Use of Syringe Exchange and Incidence of Viral Hepatitis Infections

Using data from a cohort study among Seattle IDUs, researchers assessed whether participation in a syringe exchange program was associated with incidence of hepatitis B (HBV) and hepatitis C (HCV) infection. Susceptible IDUs included 187 who were seronegative for HCV and 460 who were seronegative for HBV between June 1994 and January 1996. They were followed for seroconversion one year later. There were 39 HCV infections and 46 HBV infections, and no apparent protective effect against either HBV or HCV from participation in the syringe exchange.

The authors hypothesize that changes in the injecting behaviors of IDUs using the syringe exchange may account for these findings. For example, needle exchange programs typically attract drug injectors who practice high risk behaviors for transmission of blood-borne infections such as more frequent injections and sharing of needles and syringes. At the same time, lower risk IDUs who don't use an exchange can get sterile syringes from pharmacies and other sources. If exchange users are at higher risk for transmission of hepatitis, this may explain why the rates of infection are higher than expected and similar to non-exchange users who may be at a lower risk of infection. Hagan, H., McGough J.P., Thiede, H., Weiss, N.S., et al. Syringe Exchange and Risk of Infection with Hepatitis B and C Viruses. *Am J Epidemiol*, 149 (3), pp. 203-213, 1999.

Very Recent and New Injectors in NYC Have Very High Risks of Acquiring the HIV Infection

This paper examines HIV risk behavior and HIV infection among new initiates into illicit drug injection in New York City. Cross-sectional surveys were conducted of IDUs recruited from a large detoxification treatment program (n=2489) and a street store-front research site (n=2630) in New York City from 1990 through 1996. The interviews covered demographics, drug use history, and HIV risk behavior; serum samples were also collected for HIV testing. Subjects were categorized into two groups of newer injectors: very recent initiates (just began injecting to 3 years of injecting) and recent initiates (injecting 4 to 6 years); and long-term injectors (injecting more than or at least 7 years). Of the 5119 study subjects, 954 (19%) were newer injectors, all of whom had begun injecting after knowledge about AIDS had become widespread among IDUs in the City. New injectors were more likely to be female and white than long-term injectors, and new injectors were more likely to have begun injecting at an older age (median age at first injection for very recent initiates, 27 years; median age at first injection for recent initiates, 25 years; these compare to the median age at first injection for long-term injectors, 17 years). Newer injectors generally matched long-term injectors in frequencies of HIV risk behavior. No significant differences were found among these groups on four measures of injection risk behavior. HIV infection was substantial among the newer injectors: HIV prevalence was 11% among very recent initiates and 18% among recent initiates. Among new injectors, African Americans, Hispanics, females, and men who had sex with men were more likely to be infected. New injectors appear to have adopted the reduced risk injection practices of long-term injectors in the City. HIV infection among new injectors, however, must still be considered a major public health problem in New York City. Des Jarlais, D.C., Friedman, S.R., Perlis, T., Chapman, T.F., et al. Risk Behavior and HIV Infection Among New Drug Injectors in the Era of AIDS in New York City. *J AIDS and Human Retrovirol*, 20(1), pp. 67-72, 1999.

Study Finds Expanded Number, Size, and Scope of Syringe Exchange Programs in the U.S.

In November 1996, researchers surveyed 101 syringe exchange programs (SEPs) and conducted telephone interviews with SEP program directors in the U.S. Data were collected on the number of syringes exchanged, SEP program operations, legal status, and services offered. The findings were compared with those of a similar survey conducted in 1994. Of the 101 SEPs contacted, 87 (86%) responded. Almost all that did not respond were small and/or "underground" (operating in states that have no prescription law and formal support from local officials). The 87 SEPs that responded operated in 71 cities in 28 states and one territory; 44 were in four states (California, New York, Connecticut, and Washington). About 14 million syringes were exchanged by the SEPs in 1996, compared to 8 million syringes by 55 SEPs in 1994. Program size was directly related to the provision of services other than syringe exchange. All 87 SEPs provided IDUs with information about safer injection techniques and/or use of bleach to disinfect injection equipment; 84 provided referrals to clients to substance abuse treatment programs, information about safer use of condoms to prevent sexual risks for HIV and other STDs; and 70 offered education about STD prevention. Just over half (46) of the SEPs were legal, 20 (23%) were illegal but tolerated, and 21 (24%) were illegal/underground. Legal programs were more likely to offer on-site HIV counseling and testing and tuberculosis testing than were other programs, and to have a steady source of funds and adequate staffing. Secondary exchange was reported as a widespread and important way to distribute sterile syringes to IDUs unable to obtain them directly from the SEP. SEPs have expanded in size, geographic distribution, numbers of syringes exchanged, and types of services offered since 1994. These changes have occurred with support from local and state governments and/or from contributions of organizations, private citizens, and volunteers, but without funding from the U.S. government. Paone, D., Clark, J., Qiuhu, S., Purchase, D., and Des Jarlais, D.C. Syringe Exchange in the United States, 1996: A National Profile. *Am J Public Health*, 89(1), pp. 43-46, 1999.

Psychoactive Drug Use Does Not Appear to Have Important Effects on the Course of HIV

Early in the history of the AIDS epidemic there was clear evidence of differences in the outcomes of HIV infection

between injecting drug users and men who have sex with men. There were also some indications that high levels of nonsterile drug injection equipment may increase the progression of the HIV infection. Recent epidemiologic studies indicate no differences in rates of progression to AIDS among drug injectors, men who have sex with men, or persons infected through heterosexual contact. In vitro and animal studies suggest that the effects of different psychoactive drugs on HIV infection may be negative, positive, or mixed, and that the effects of a psychoactive drug on immune functioning may differ among acute administration, chronic administration, or cessation of chronic administration. Although the current epidemiologic data do not provide support for the hypothesis that psychoactive drug use will have any important effects on the course of HIV infection, possible interactions between psychoactive drugs and antiviral medications and medication adherence issues among drug users are important and promising areas for AIDS research. Des Jarlais, D.C. Psychoactive Drug Use and Progression of HIV Infection. *J AIDS and Human Retrovirol*, 20(3), pp. 272-274, 1999.

Gender Differences in an Impoverished Minority Population

Gender differences among impoverished minority females (n = 205; 87% African-American, 13% Latina) and males (n = 203; 89% African-American, 11% Latino) were examined using associations among latent variables representing stress, self-esteem, avoidant and active coping strategies, and health outcomes of depression, escapist drug use, and sexual risk behaviors. Subjects were selected from individuals participating in a community-based educational AIDS prevention program in 9 homeless shelters and 11 residential drug recovery programs in Los Angeles. Among both men and women, drug use and depression were positively related to each other. A large and significant relationship between stress and sexual risk behaviors among women was not evidenced for men. In multiple group latent means comparison models, women reported significantly more stress, depression, and avoidant coping styles than men. In predictive path models, an avoidant coping style predicted escapist drug use among men whereas greater stress predicted escapist drug use among women. Greater stress, and lower self-esteem predicted depression in both groups. Greater stress and less active coping predicted more sexual risk behaviors for women. No predictor construct in this model was significantly associated with elevated sexual risk behavior among the men. These results suggest gender-specific leverage points for AIDS-risk reduction interventions. Stein, J.A., and Nyamathi, A. Gender Differences in Relationships Among Stress, Coping, and Health Risk Behaviors in Impoverished Populations. *Personality and Individual Differences*, 26, pp. 145-157, 1999.

Higher Levels of HIV Risk Behaviors Found in IDUs Who Use Crack vs. Those Who Don't

The baseline characteristics and HIV risk behaviors were compared in two groups of out-of-treatment IDUs in South Philadelphia, one of 366 IDUs who concurrently smoked crack (smoking IDUs) and one of 212 IDUs who did not smoke crack in the past 30 days. Temporal trends in recent risk behaviors were also assessed for each drug user group over an 18-month period, January 1992 to June 1994. Although both groups were economically disadvantaged and at high risk of HIV infection, smoking injectors had fewer economic resources and were at a moderately greater risk of HIV because of higher levels of sexual risk behaviors and higher rates of ever having an STD compared to IDUs only. Analysis of temporal trends revealed few reductions in drug risk behaviors and none in sexual risk behaviors. This study points to the need for examining differences between types of drug users. Understanding the characteristics of different types of drug users and their communities is essential to develop tailored, maximally effective interventions and appropriate treatment programs for persons who use multiple drugs. Semaan, S., Kotranski, L., Collier, K., Lauby, J., et al. Temporal Trends in HIV Risk Behaviors of Out-of-Treatment Injection Drug Users and Injection Drug Users Who Smoke Crack. *J AIDS and Human Retrovirol*, 19, pp. 274-281, 1998.

Risk Behavior Change in HIV Positive and HIV Negative Drug Users

This research sought to examine the effectiveness of an HIV intervention program among out-of-treatment IDUs and crack users who were HIV+ and HIV-, and to identify risk behaviors of seropositive drug users that may require more intensive or targeted intervention efforts. A total of 225 IDUs (31% HIV+) and 316 crack users (15% HIV+) were administered a baseline interview, received HIV testing and test results, and participated in a 6-month follow up interview. There were significant differences between injectors and crack smokers by demographic characteristics: injectors were more likely to be Puerto Rican and crack smokers more likely to be African American; injectors were more likely to be male, and living on the street or in a shelter. About 40% of both groups were homeless, only 5% were employed, and illegal activity was the primary source of income for 46% of the injectors and 23% of the crack smokers. Injectors were significantly more likely to be HIV+ than crack smokers. Both HIV-positive and negative drug users reported reductions in risk behaviors over time. For both injection-related and sex-related risks, seropositive

subjects reported significantly greater reductions from baseline to follow-up than seronegatives. It appears that seropositives may have already reduced risk behaviors based on knowledge of their serostatus at baseline, underscoring the utility of HIV testing and counseling; i.e., knowledge of serostatus can lead to reductions in sex- and injection-related risks. The researchers also suggest that the changes in risk behaviors in the drug users may have been influenced by multiple factors, including participation in the intervention study, receiving pre- and post- HIV test counseling, and benefiting from community-wide outreach efforts and more widely available needle exchange programs. Deren, S., Beardsley, M., Tortu, S., and Goldstein, M. HIV Serostatus and Changes in Risk Behaviors Among Drug Injectors and Crack Users. *AIDS and Behavior*, 2(2), pp. 171-176, 1998.

Older Substance Abusers, Age-Related Factors, and HIV/AIDS

A study was conducted to examine the role of HIV counseling, testing, and partner notification in the lives of street addicts of all ages, with a subsample of the addicts being older injectors (N=53) ranging between 50 to 86 years. About 75% of the sample were African American and the rest were White or Latino; there were 11 women and 42 men. Ten of the 53 (19%) were positive for HIV. Six of the 10 seropositive IDUs lived alone, compared to only nine of the 43 seronegative IDUs. Heroin was the drug of choice, and one injection a day was the average. All of the IDUs reported polydrug use, with the major drugs used being downers, amphetamines, and cocaine. Six of the seven males who were HIV positive had been crack smokers at one time or another. All but one of the women and half the men reported having had heterosexual sex in the past six months, but nearly 60% said they never used a condom. A lot of time was spent by the IDUs to procure drugs and money to buy drugs, by stealing, engaging in "street hustles," or by assisting drug dealers in supplying their customers. The paper reviews issues related to the illness trajectory for HIV/AIDS in older drug users, social support and social networks, access to old age benefits and public assistance, and the need for age appropriate interventions to facilitate older drug users to adopt strategies of risk reduction and AIDS prevention. Levy, J.A. *AIDS and Injecting Drug Use in Later Life. Research on Aging*, 20(6), pp. 776-797, 1998.

Unprotected Sex Among Drug-Using Men and Women

Using the AIDS risk reduction model as a conceptual framework, a multivariate prospective test of psychosocial antecedents of unprotected sex was conducted using 155 female and 134 male heterosexual injection drug users. For both women and men, stronger intentions to use condoms predicted subsequent reduction in unprotected sex. For women, but not men, higher perceived self-efficacy also led to reductions in unprotected sex. These results suggest that explicit formation of risk-reduction intentions is an important antecedent to sexual behavior change by drug users of either gender and that change by drug-using women is also influenced by their perceived control over sexual risk-taking. Longshore, D., Stein J.A., Anglin, M.D., and Kowalewski, M.R. *Psychosocial Antecedents of Unprotected Sex by Drug-Using Men and Women. AIDS & Behavior*, 2, pp. 293-306, 1998.

Two-index Method for Evaluating Models

This article extends work on the use of fit indices to evaluate models, and proposes use of a two-index evaluation strategy based on the standardized root mean squared residual and supplementing it with one of several well-known indices. A series of empirically determined cut-off values are developed for the various indices to replace ad-hoc rules such as the requirement that a model fit exceed an arbitrary value (e.g., .9) before the model is considered adequate. It was determined that a cutoff value closer to .95 for several indices is required before one can conclude that there is a relatively good fit between the hypothesized model and the observed data. The proposed two-index presentation strategy is required to reject reasonable proportions of various types of true-population and misspecified models. This work will ultimately lead to the development of improved statistical models (such as structural equation models) used in drug abuse research. Hu, L. and Bentler, P.M. *Cutoff Criteria for Fit Indices in Covariance Structure Analysis: Conventional Criteria Versus New Alternatives. Structural Equation Modeling*, 6, pp. 1-55, 1999.

Correlates of High Risk Sexual Activity Are Identified Among STD Patients Who Use Crack

Crack-smoking sexually transmitted disease (STD) patients are at high-risk for contracting HIV. To examine the effects of cocaine use and other correlates on high-risk sexual behavior among STD clinic patients, a cross-sectional study was conducted. The sample included 1,490 consecutive patients attending three Los Angeles County STD clinics between 1992 and 1994. Logistic regression analysis found high-risk sexual activity was associated with being male and of younger age. Among women, high-risk sexual behavior was associated with crack cocaine use and a perceived

need for help. Among men in the study, ethnicity (being black) and having an arrest history were associated with high-risk behavior. Effective intervention strategies should address cocaine use among STD patients and provide them with referrals to drug treatment. Hser, Y.I., Chou, C.P., Hoffman, V., Anglin, M.D. Cocaine Use and High-Risk Sexual Behavior Among STD Clinic Patients. *Sex Transm Dis*, 26(2), pp. 82-86, 1999.

Computer-Assisted HIV Risk Assessment Interviewing is Acceptable to Drug Users

Researchers assessed the acceptability of a computer HIV risk assessment instrument administered to not-in-treatment drug users. The study differed from other assessments of the acceptability of computer-assisted data collection in that the population of interest had relatively little experience in use of computers and only limited education. The study was also implemented under field conditions. Three questions were asked related to acceptability (are drug users comfortable responding to HIV risk questions using the computer assessment; do they feel they possess the requisite skills to respond to questions using a computer; and do they believe that their responses will remain private and confidential). Only slight modifications were made to the content of the instrument. Data collection was facilitated using audio enhancement and touch screen, and three scales were used to measure comfort, skill, and perceived privacy. The findings suggest that drug users are comfortable responding to an HIV risk assessment using computer assisted interviewing. Drug users perceived they possessed the requisite skill to successfully complete the interview. Study participants also reported that they believed their responses would remain private and confidential. Their favorable attitudes seemed to be in evidence even though some of the questions were lengthy for some of the respondents. The average time for completing the risk assessment was 60 minutes. The results of this study suggest that computer interviewing has potential for collecting HIV risk information from drug users under field conditions, even though conditions in field settings are often far less manageable than conditions in clinical or institutional settings. Williams, M.L., Freeman, R.C., Bowen, A.M., and Saunders, L. The Acceptability of a Computer HIV/AIDS Risk Assessment to Not-In-Treatment Drug Users. *AIDS Care*, 10 (6), pp. 701-711, 1998.

Results of the Cooperative Agreement Studies Indicate Intervention Efficacy

In this article, researchers examine the NIDA Cooperative Agreement HIV intervention studies for active drug users relative to the constructs of prevention efficacy and effectiveness. Conservatively interpreting the outcome findings indicates they fall within the domain of efficacy rather than effectiveness, owing to the high degree of control and organization that occurred with respect to intervention recruitment, participation, process monitoring, and staff training. Because the interventions were implemented and evaluated in community-based, noninstitutional settings with many real-world constraints, minimal shrinkage of their effects would occur if they were implemented in uncontrolled community settings. The CA intervention studies also have attributes of structure, content, process, dose, and participant characteristics that are related to intervention efficacy. Rhodes, F., Wood, M.M., and Booth, R.E. Efficacy and Effectiveness Issues in the NIDA Cooperative Agreement: Interventions for Out-of-Treatment Drug Users. *J Psychoactive Drugs*, 30(3), pp. 261-269, 1998.

Building Bridges for Community Involvement in Drug and HIV Research among Minority Populations

This paper proposes methods for developing a community base for drug abuse research with minority populations. Recommendations are based on 6 years of research in communities with a high prevalence of prostitution and/or drug use in New York City and Atlanta. Researchers employed a qualitative methodology that included participant observation, in-depth interviewing, and focus groups. The participant observation involved data collection in the subjects' natural setting. The main stages in participant observation, also referred to as ethnographic mapping, were to gain access, develop a role in the field, identify key respondents, and build trust relationships. The open-ended structured interviews facilitated the development of trust and permitted discovery of the subjects' perspective of his/her own salient issues. Sterk, C.E. Building Bridges: Community Involvement in Drug and HIV Research Among Minority Populations. *Drugs & Society* 14, 1/2, pp. 107-121, 1999.

Incidence and Duration of Hospitalizations Among Persons with AIDS: An Event History Approach

The hospitalization patterns of persons with AIDS (PWAs) in a multi-state/multi-episode continuous time duration framework were examined using Medicaid claims history data from 1,401 AIDS patients in New Jersey. Differences in the use of inpatient services by race/ethnicity, gender, AIDS risk group, region, severity of illness, and year of

services were studied. Participation in a Medicaid waiver program offering case management and home health care was associated with hospital stays 1.3 days shorter than non-participants. African-American race and Hispanic ethnicity were associated with hospital stays 1.2 days and 1.0 day longer respectively than for non-Hispanic whites. African Americans also experienced more frequent hospital admissions. Residents of the high HIV-prevalence area of the state had more frequent admissions and stays two days longer than those residing elsewhere in the state. Older PWAs experience less frequent hospital admissions but longer stays, with hospitalizations of 55-year-olds lasting 8.25 days longer than those of 25-year-olds. Crystal, S., Lo Sasso, A.T., & Sambamoorthi. Health Services Research 33(6), pp. 1611-1638, February 1999.

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National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

May, 1999

Research Findings

Epidemiology, Etiology, and Prevention Research

In the Past 6 Months

- Heroin has attracted a growing number of young people, many from the suburbs, some of whom inject.
- Marijuana indicators have continued to escalate across the country.
- Cocaine indicators have generally continued to level or decline, but some increases are reported.
- Methamphetamine has been increasingly involved in medical emergencies across the country, but other indicators are mixed.
- "Club drugs," especially GHB, have increasingly resulted in adverse reactions in several areas.

The 45th biannual meeting of the **Community Epidemiology Work Group (CEWG)** was held in Miami, Florida on December 15-18, 1997.

The CEWG is composed of researchers from 21 metropolitan areas of the United States who meet semiannually to report on patterns and trends of drug abuse in their respective areas; emerging drugs of abuse; vulnerable populations and factors that may place people at risk of drug use and abuse; and, negative health and social consequences. Reports are based on drug abuse indicator data, such as morbidity and mortality information, treatment data, and local and State law enforcement data. Additional sources of information include criminal justice, correctional, medical and community health reports, local and State surveys, and research findings from ethnographic studies. The following are highlights from the meeting:

- **Cocaine** - While most cocaine indicators continue to reflect declines or stability, some increases are still reported. Cocaine mortality figures declined or appeared stable in eight cities but increased in three areas (Detroit, Phoenix, and Texas) where 1997 or partial-1998 data were available. Emergency department (ED) mentions declined significantly* in 6 of the 20 CEWG cities in the Drug Abuse Warning Network (DAWN) and increased* in 2 (Chicago and Denver). The percentage of treatment admissions for primary cocaine problems declined or remained stable in 15 of the 16 areas where trend data were available (it increased in Philadelphia). Cocaine-positive urinalysis percentages remained relatively stable (within 4 percentage points) among male adult arrestees in 16 of the 17 CEWG cities in the Arrestee Drug Abuse Monitoring (ADAM) program. Again, an increase** in Philadelphia was the exception. The cocaine-using population generally continues to age; however, younger users are still appearing in local indicators in Dallas (ED mentions), Miami, and Washington, DC (arrestee urinalysis). Austin street outreach workers report a new generation of young African-American crack addicts and an increase in crack users among Hispanic women. Injection of crack (dissolved in lemon juice, orange juice, or vinegar) is reported in Austin, Boston (usually in conjunction with heroin), New York, and Washington, DC (either alone or mixed with heroin).

Some slight shifts to cocaine hydrochloride are reported: in Detroit (with increased intranasal use), in cities outside of Boston (possibly in relation to cocaine injection), and in San Francisco. In areas such as Atlanta, the crack scene is shifting to suburban and rural counties.

- **Heroin** - Mortality figures suggest an abatement or plateau following increases: between 1996 and 1997, heroin-related deaths increased in 8 of the 11 cities where such data were available; but partial-1998 data, available in 8 cities, suggest declines or stable levels in 6 of them. DAWN and treatment figures show more mixed trends: ED mentions increased* in four cities (Miami, New Orleans, Chicago, and Washington, DC) and declined* in three (Los Angeles, Baltimore, and New York); and primary heroin treatment percentages increased slightly in four cities (Boston, Detroit, New Orleans, and New York), declined in five (Los Angeles, Philadelphia, San Diego, San Francisco, and Seattle), and remained stable in five (Denver, Atlanta, Minneapolis/St. Paul, St. Louis, and Dallas). ADAM percentages remained generally stable, except for an increase** in Philadelphia.

Researchers caution against complacency about the recent leveling of some indicator data because there is lag time between heroin initiation and its appearance in indicators. National concerns about the lure of "heroin-chic" trends and the "normalization" of heroin among middle-class youth appear to be borne out in some cities. San Francisco ethnographers report an increase in young middle-class users. Younger populations are also increasingly initiating heroin use in Boston, where needle exchange workers report a recent increase in younger injectors. Atlanta ethnographic reports also continue to indicate an increasing number of recently initiated snorters shifting to injection. An increase in injecting among Newark treatment admissions suggests a possible reversal of the trend toward increased snorting which started in the mid-1980s. A Chicago study identified a high percentage of suburban youth who are injectors. Suburban or rural heroin activity is also reported around the Baltimore and Boston areas. A recent surge in asthmatic reactions among young heroin snorters is under investigation in Chicago.

- **Marijuana** - Marijuana now accounts for more than 10 percent of total ED mentions in six cities, and it is the top-ranking primary drug treatment problem in four cities (Denver, Seattle, New Orleans, and Minneapolis/St. Paul). ED mentions increased* in six cities; no significant declines were noted. Treatment percentages increased in 10 cities and remained stable in 5. Among adult male arrestees, marijuana-positive findings exceeded cocaine-positives in nine ADAM cities; percentages declined in three cities and increased in two**. In each of the eight CEWG cities where ADAM tests juvenile males, the percentage of positive urinalyses was much higher for juveniles than for adults. Focus group findings in Boston revealed teens who, because they had grown bored with or developed tolerance for marijuana, had moved on to other drugs. Marijuana is sometimes combined with crack in Chicago (3750s), Miami (geek joints), and Philadelphia (turbos); with PCP in Chicago (wicky stick or donk), New York (high-powered blunts), Philadelphia (love boat), and St. Louis; with methamphetamine in St. Louis; with embalming fluid in Minneapolis and Seattle; and with embalming fluid laced with PCP in Houston. The World Wide Web has become a substantial source of information, including instructions on indoor growing, user group discussions, announcements about the "legal" sale of marijuana, and advertisements for marijuana seeds.
- **Stimulants** - Indicators of **methamphetamine** use are mixed. Available partial-1998 mortality figures show methamphetamine-related deaths declined in four cities and increased in two (Phoenix and St. Paul). Methamphetamine ED mentions increased* in nine cities, in all regions of the country: Atlanta, Dallas, Denver, Minneapolis/St. Paul, Philadelphia, Phoenix, San Diego, San Francisco, and Seattle; no significant declines were noted. Methamphetamine remains the number-one primary drug treatment problem in San Diego and Honolulu. Treatment percentages increased in four western cities (Denver, San Diego, San Francisco, and Seattle) and remained stable in four (Dallas, Los Angeles, Minneapolis/St. Paul, and St. Louis). Methamphetamine-positive urinalyses remained generally stable** among adult male arrestees. "Tweaking," or "crystal" use, occurs among a broad array of subcultures, including urban gay men, white working-class, bikers, the dance club scene, adolescent girls, and urban runaway street youth who follow a yearly circuit ranging from New Orleans, the Southwest, California, and the Northwest (including Vancouver, British Columbia).
- **Methylenedioxymethamphetamine** - MDMA (ecstasy, blue lips, blue kisses, and white dove) availability is reported, primarily as a club drug at raves and dance parties, in Atlanta, Baltimore, Boston, Chicago, Miami, New York, St. Louis, Seattle, and Washington, DC. In the Boston area, the prominence of MDMA has increased as reflected in seizure data, in focus group reports by suburban white teens, in reports by needle exchange workers, and in school survey data. MDMA has now become included in Atlanta's weekend-long gay male party circuit. In Seattle, ecstasy is mixed with other drugs, such as LSD (candy flipping), mushrooms (flower flipping), and heroin (H-bomb); a new liquid form of ecstasy in that city is of concern because its purity ranges wildly, it is cut with many different drugs, and users are uncertain of what they are getting. Similarly, in Miami, adulteration is viewed as an opportunity to try something different rather than a ripoff, a phenomenon known as "rolling" because these combinations produce seesaw stimulant and depressant effects.

- **Methylphenidate** (Ritalin) remains readily obtainable by Boston students in middle- and upper-middle-class communities; it is increasingly reported in Phoenix in poison control calls; and a resurgence is reported in Seattle, where it is diverted from prescribed use, especially among younger students.
- **Depressants** † Use of **Gamma-hydroxybutyrate** (GHB), a central nervous system depressant, continues to spread across the country with recipes for its manufacture easily accessible on the Internet. It has been involved in poisonings, overdoses, date rapes, and even fatalities in Boston, Colorado, Detroit, Miami, New York, Phoenix, Seattle, and Texas. Availability is also reported in Atlanta, Baltimore, and Minneapolis/St. Paul. It is associated with the club scene, raves, gay circuit parties, and fitness centers and gyms. It is frequently consumed with alcohol, and sometimes with marijuana, LSD, or ecstasy. In New Orleans, it is mixed with amphetamine in an alcoholic drink called "max." Only in San Francisco did ethnographers report a decline in 1998. Its names include "grievous bodily harm," "cherry meth," "easy lay," "gamma," "Georgia home boy," "G," "liquid E," "liquid ecstasy," "liquid X," "great hormones at bedtime," "everclear," "g-riffic," and "salty water." In addition, **gamma butyrolactone** (GBL) is contained in commercial products (Blue Nitro, RenewTrient, and ReVivarin) legally sold as health supplements; it metabolizes into GHB and produces clinical symptoms identical to GHB. Dangerous labeling may cause a critical lag time in seeking help for GBL toxicity.

Another club drug, **ketamine** ("Special K" or "vitamin K"), is popular in cities such as Atlanta, Boston, Miami, Minneapolis/St. Paul, San Diego, and Seattle. It is usually snorted, but injection is reported among young users in some areas, including Boston and Minneapolis/St. Paul. In the latter city, being under the influence of ketamine is known as being "in the hole" or "in the K hole." The drug has been involved in DUI cases and poison control calls in Miami and in one death in San Diego.

- **Clonazepam** - (Klonopin or Rivotril) has been termed "street drug of the 90s" in Boston. Juveniles in Texas commonly use it in combination with beer. It is sold in Atlanta to enhance the effects of methadone, and it is commonly diverted in Phoenix. **Alprazolam** (Xanax, or "sticks") is increasingly replacing diazepam on the street in New York; it is also a common street drug in Boston. **Diazepam** is appearing in Atlanta crack houses. An emerging trend in Seattle involves concomitantly injecting heroin and a depressant, typically diazepam - a longtime practice in Chicago. **Flunitrazepam** (Rohypnol) reports continue to decline in Miami, but still appear in Minnesota and in Texas treatment and survey data. Use of this "date-rape" drug was suspected in a syphilis outbreak among white, middle-class adolescent girls in Atlanta. **Trazodone** (Desyrel) has been involved in numerous poisonings and one death in Detroit.
- **Hallucinogens** - Ethnographic, law enforcement, and survey data suggest continued low-level abuse of lysergic acid diethylamide (LSD) and phencyclidine (PCP), despite declining or stable ED and treatment indicators. For example, treatment percentages have been declining in Chicago for more than a decade, but school survey data suggest some increases in LSD. Massachusetts school surveys also show increased hallucinogen use. LSD is reportedly common among teens and young adults - often in suburban and rural settings in a number of cities, including Atlanta, Baltimore, Boston, Detroit, Minneapolis/St. Paul, New York, St. Louis, Seattle, and parts of Texas. It is frequently found at local concerts, parties, and raves. PCP availability continues in several cities, including Baltimore, Minneapolis/St. Paul, New Orleans, and New York. Ethnographers in San Francisco note a renewed interest in PCP in one predominately Hispanic neighborhood. In Washington, DC, PCP-positive screens among adult and juvenile arrestees continue their decade-long decline. Use of PCP in combination with marijuana continues to be reported in Chicago, New York, Philadelphia, and St. Louis. PCP/crack combinations are reported in Philadelphia. In Houston, marijuana cigarettes are dipped in embalming fluid containing PCP. Psilocybin mushrooms ("shrooms") are reportedly available in some cities, including Baltimore, Minneapolis/St. Paul, and Seattle.
- **Other Drugs** - Ten Newark teenagers were recently hospitalized for reactions to **jimsonweed**; the drug is also reportedly abused in Phoenix. Ingesting **cough medications** in Minneapolis/St. Paul is known as "robo tripping" and adolescents who use it are known as "robo cops." The practice has resulted in adverse reactions. The cough medicine guaiphenesin (Robitussin) is also reportedly abused in Phoenix and by Boston teenagers.

*DAWN comparisons are for first half 1996 versus first half 1997; changes are noted only when statistically significant at $p < 0.05$.

**ADAM comparisons are for first half 1997 versus first half 1998; changes are noted only when they are > 5 percentage points.

Posttraumatic Stress Disorder and Drug Use Disorders

This study sought to elucidate the relationships between posttraumatic stress disorder (PTSD), trauma, and drug use disorders. Although much comorbidity between PTSD and drug abuse has been observed, the causal mechanisms have remained unclear. This paper presents data on 1007 adults, ages 21-30, enrolled in a health maintenance organization in Michigan. The subjects were followed up three and five years after initial interview, and assessed for PTSD, drug use disorders, and traumatic events. While PTSD increased the risk for drug abuse or dependence, exposure to trauma in the absence of PTSD did not. Risk was particularly notable for abuse or dependence on prescription drugs. Prior drug abuse or dependence did not appear to increase the risk for trauma or PTSD in this sample. It appears that drug abuse or dependence in individuals with PTSD may be a result of self-medication, although it is also possible that there is a shared vulnerability to PTSD and drug use disorders. Chilcoat, H.D., and Breslau, N. *Arch Gen Psychiatry*, 55, pp. 913-917, 1998.

Preventing Adolescent Health Risk Behaviors By Strengthening Protection During Childhood

Researchers at the University of Washington examined the long-term effects of an intervention combining teacher training, parent education, and social competence training for children during the elementary grades on health-risk behaviors at age 18 years. The study employed a nonrandomized controlled trial with follow-up six years after intervention. Subjects consisted of 643 students in public elementary schools serving high-crime areas in Seattle, Washington. A full intervention condition (n=156) provided in grades 1 through 6 consisted of 5 days of teacher in-service training each intervention year, developmentally appropriate parenting classes offered to parents when children were in grades 1, 2, 3, 5, and 6, and developmentally adjusted social competence training for children in grades 1 and 6. A late intervention condition (n=267) provided in grades 5 and 6 paralleled the full intervention at these grades. A control condition (n=220) consisted of students in schools assigned to receive no intervention in grades 5 and 6 and who were not in intervention classrooms in grades 1 through 4. The follow-up at age 18, six years after the end of intervention, included 93% of the baseline sample and assessed self-reported substance use, violent and non-violent crime, sexual activity, pregnancy, bonding to school, school achievement, grade repetition and school dropout, suspension and/or expulsion, and school misbehavior. Compared to control students, fewer students receiving the full intervention reported heavy drinking (15.4% vs. 25.6%), violent delinquent acts (48.3% vs. 59.7%), sexual intercourse (72.1% vs. 83.0%), having multiple sex partners (49.7% vs. 61.5%), and pregnancy or causing pregnancy (17.1% vs. 26.4%) by age 18 years. The full-intervention student group reported more commitment and attachment to school, better academic achievement, and less school misbehavior than control students. Late intervention in grades 5 and 6 only did not significantly affect health-risk behaviors in adolescence. These findings suggest that a package of interventions with teachers, parents, and children provided throughout the elementary grades can have enduring effects in reducing heavy drinking, violent behavior, and sexual intercourse at age 18 years among multiethnic urban children. Results support efforts to reduce health-risk behaviors through universal interventions in selected communities or schools serving high-crime neighborhoods. Hawkins, J.D., Catalano, R.F., Kosterman, R., Abbott, R., Hill, K.G. *Archives of Pediatrics and Adolescent Medicine*, 153, pp. 226-234, 1999.

A Longitudinal Study of Children of Alcoholics: Predicting Young Adult Substance Use Disorders, Anxiety, and Depression

Investigators at Arizona State University tested the magnitude and specificity of parental alcoholism effects on young adult alcohol and drug abuse/dependence, and also tested whether adolescent symptomatology and adolescent substance use mediated the effects of parental alcoholism on these diagnoses. Participants were from an ongoing longitudinal study in which a target child was assessed in adolescence using computer-assisted interviews with both parents and the child, (N=454 families, mean age at Time 1=12.7). In young adulthood, the original target children and their full-biological siblings were assessed (mean age=21) again using computer-assisted interviewing (N=732 young adults). Results showed unique effects of parent alcoholism on young adult substance abuse and dependence, over and above the effects of other parental psychopathology, suggesting that parent alcoholism is a specific risk factor for substance abuse/dependence above and beyond the general elevation in risk that might be associated with having a dysfunctional parent. Adolescent externalizing symptoms were found to be significant mediators of these effects, suggesting that children of alcoholics are at elevated risk for substance use disorders, in part, because of their broader pattern of early adolescent antisociality and conduct problems. Drug and alcohol diagnoses were mediated somewhat differently. For drug abuse/dependence diagnoses, adolescent conduct problems completely explained the significant parent alcoholism effect, although an effect of parental antisociality remained. However, for alcohol abuse/dependence diagnoses, the effects of parental alcoholism could not be completely explained by adolescent conduct problems. Thus, greater vulnerability to the psychopharmacological properties of alcohol may account for additional risk for alcoholism among children of alcoholics, whereas parental antisociality is more

important to drug abuse/dependence because drug use necessarily involves illegal behaviors. Chassin, L., Pitts, S.C., DeLucia, C., and Todd, M. *Journal of Abnormal Psychology*, 108, pp. 106-119, 1999.

Marijuana Use Among American Indian Adolescents

Researchers at the University of Colorado Health Sciences Center report two studies of marijuana use among American Indian adolescents. The first study examined the characteristics of marijuana (MJ) users in a survey of 1464 9th-12th-grade adolescents from four Indian tribal groups. Forty percent of these American Indian subjects had used MJ at least once in the last month. The prevalence of MJ use varied across the 4 tribes. Low- and high-frequency marijuana use (1-3 times in the past month, and 11 or more times in that period, respectively) were modeled as outcome variables. The factors associated with MJ use varied with the frequency of use and by gender. Males were no more likely than females to use MJ at a low frequency, but were more likely to use at high frequency. In the final multivariate models, low-frequency MJ use among females was associated with reporting that peers encouraged alcohol use as well as use of alcohol and stimulants. Among males, low-frequency use was associated with greater positive alcohol expectancies, lower grades in school, and alcohol use. While high-frequency MJ use was associated with use of alcohol, stimulants and cocaine among females, such use was associated with higher scores on the antisocial behavior scale as well as the use of alcohol, stimulants and cocaine among males. Overall, the strongest associations were with the use of alcohol and other illicit substances. Novins, D.K. and Mitchell, C.M. Factors Associated With Marijuana Use Among American Indian Adolescents. *Addiction*. 93(11), pp. 1693-1702, Nov 1998. The second study examined the developmental course of marijuana use among 1766 American Indian adolescents 14-20 years old across three cultural groups. Three annual ascertainment of 30-day marijuana use and 5 age cohorts were linked and hierarchical linear modeling was used to assess the trajectory of marijuana use, taking account of gender and community group differences as well. Use of marijuana increased in middle adolescence, peaked in later adolescence, and began to decrease in early adulthood, supporting a non-linear maturational model. Both gender and community differences were observed in the trajectories, with girls and boys similar in frequency of use at age 14 but diverging by age 20; in all three communities, males showed a sharper increase in use. The authors conclude that growth curve analysis provides an additional tool for studying effects of interventions that may not be apparent in traditional evaluation design. Mitchell, C.M., Novins, D.K., and Holmes, T. Marijuana Use Among American Indian Adolescents: A Growth Curve analysis from Ages 14 Through 20 Years. *Journal of the American Academy of Child and Adolescent Psychiatry*, 38(1), pp. 72-78, 1999.

Stress-Coping Factors in Adolescent Substance Use: Test of Ethnic and Gender Differences in Samples of Urban Adolescents

Addressing the question of whether and how the etiology of drug use differs for adolescents in various ethnic groups, researchers investigated group differences in the relationship between stress-coping variables and substance use with samples of inner-city students in 6th-8th grades (N = 1,289) and metropolitan-area students in 7th-9th grades (N = 1,702). Use of cigarettes, alcohol, and marijuana were considered, and measures of psychosocial predictor domains focused on affect, life events, parental support, and coping patterns. African-American adolescents had the lowest rate of substance use, Hispanics were intermediate, and Whites had the highest rate; there was no gender difference in overall substance use. Multiple regression analysis showed that the strength of predictive relationships for stress-coping variables was lower for African Americans and was greatest for Whites; methodological tests showed that these differences were not attributable to statistical artifacts. Hispanic adolescents showed greater vulnerability than did Whites at younger ages but this effect was reversed at later ages. Implications of the study include the importance of incorporating stress-coping components in the design of prevention programs for all ethnic groups. As affective factors were less predictive of substance use among African-American adolescents, programs should give greater attention to other domains when targeting programs to these adolescents. Earlier prevention efforts (before age 12) are likely to be most critical for Hispanic youth. Vaccaro, D. and Wills, T.A. *Journal of Drug Education*. Vol. 28(3), pp. 257-280, 1998.

Illicit Substance Use Among Adolescents: A Matrix of Prospective Predictors

A research team led by Dr. John Petraitis reviewed findings from 58 prospective studies of illicit substance use (ISU) among adolescents. In addition to including only longitudinal studies, the review considered both significant and nonsignificant findings, focused on relationships for which cross-study validation was possible, and attempted to cover the full range of predictors. Traditional review techniques were used rather than meta-analysis because of the number and range of predictors. The review identified 384 findings and classified them according to three types of

influence (social, attitudinal, and intrapersonal) and four levels of influence (ultimate, distal, proximal, and immediate). The bulk of evidence reconfirmed the importance of several predictors of ISU (e.g., intentions and prior substance-related behavior, friendship patterns and peer behaviors, absence of supportive parents, psychological temperament), revealed that a few variables thought to be well-established predictors may not be (e.g., parental behaviors, parental permissiveness, depression, low self-esteem), and uncovered several variables where findings were either sparse or inconsistent (e.g., the role of public policies concerning ISU, mass media depictions of ISU, certain parenting styles, affective states, perceptions of parental disapproval for ISU, and substance-specific refusal skills). Among the well-established findings: (1) ISU rarely is the first problem occurring among adolescents but more often follows other problem behaviors; (2) adolescents usually are prepared cognitively for ISU, usually believing that potential benefits exceed potential costs, etc; (3) ISU usually occurs after exposure to other substance users; (4) ISU is closely related to deviant peer bonding and, to a lesser extent, to detachment from and rebellion against religion, school, and family; (5) ISU occurs more frequently among adolescents who do not control their emotion, when they are extraverted and socially disinhibited, and when they are aggressive around other people -- not among those who are anxious, depressed, or low in self-esteem; and (6) though parental permissiveness seems to have little effect on ISU, absence of parental emotional support or absence of an intact family may lay the foundations for ISU. Petraitis, J., Flay, B.R., Miller, T.Q., Torpy, E.J., Greiner, B. *Substance Use & Misuse*. 33(13), pp. 2561-2604, Nov 1998.

Familial Backgrounds and Risk Behaviors of Youth with Throwaway Experiences

Some homeless youth have been characterized as "throwaway" in that they have specifically been told to leave home. In this study conducted by Research Triangle Institute, throwaway experiences among homeless youth are examined in two national samples: a nationally representative sample of youth residing in youth shelters, and a purposive sample of street youth in 10 cities. Prevalence of throwaway experiences for the total samples and for demographic subgroups is provided along with comparisons of the familial backgrounds and high-risk behaviors of youth with and without such experiences. Youth with throwaway experiences constituted nearly half of each sample. In both samples, these youth were more likely than youth without such experiences to report: (1) that they had attempted suicide, used marijuana and other drugs (excluding cocaine), and had been involved in the drug trade and carried hidden weapons; (2) that other family members had used illicit drugs during the 30 days before the youth left home; and (3) that they had spent at least 1 night away from home due to physical and/or emotional abuse or neglect, familial conflict, and familial substance use. Results indicate that throwaway youth constitute a particularly vulnerable subpopulation of homeless youth and suggest that a greater recognition and understanding of such youth will facilitate design of services that better address their needs. Ringwalt, C., Greene, J., Robertson, M. *Journal of Adolescence*. 21(3) 241-252, 1998.

Comorbidity of Substance Use Disorders with Mood and Anxiety Disorders: Results of the International Consortium in Psychiatric Epidemiology

This study is a cross-national investigation of patterns of comorbidity between substance use and psychiatric disorders in six research sites in five countries. All sites used comparable measures of substance use, and substance and mental disorders. The investigators report that there was a strong association between mood and anxiety disorders, as well as conduct and antisocial personality disorder, with substance disorders at all sites. The results also suggest that there is a continuum in the magnitude of comorbidity as a function of the spectrum of substance use category (use, problems, dependence) as well as a direct relationship between the number of comorbid disorders and increasing levels of severity of substance use disorders. This relationship was particularly pronounced for drugs. Whereas there was no specific temporal pattern of onset for mood disorders in relation to substance disorders, the onset of anxiety disorders was more likely to precede that of substance disorders in all countries. Results illustrate the contribution of cross-national data to understanding the patterns and risk factors for psychopathology and substance use disorders. *Comorbidity of Substance Use Disorders with Mood and Anxiety Disorders: Results of the International Consortium in Psychiatric Epidemiology*. Merikangas, K., Mehta, R., Molnar, B., Walters, E., Swendsen, J., Aguilar-Gaziola, S., Bijl, R., Borges, G., Caraveo-Anduaga, J., Dewitt, D., Kolody, B., Vega, W., Wittchen, H., and Kessler, R. *Addictive Behaviors*, 23(6), pp. 893-907, 1998.

Eight-fold Increased Risk of Drug Disorders among Relatives of Probands with Drug Disorders

Merikangas and her colleagues at Yale Genetics Research Unit performed a controlled family study of probands (N=231 probands; N=61 control probands; and N=1267 adult first-degree relatives) with several different predominant drugs of abuse, including opioids, cocaine, cannabis, and/or alcohol. Diagnostic estimates were based on

semistructured diagnostic interviews and/or structured family history interviews regarding each proband, spouse, and adult first-degree relative. Interview data were reviewed blindly and independently by clinicians with extensive experience in the evaluation and treatment of substance use disorders. There was an 8-fold increased risk of drug disorders among the relatives of probands with drug disorders across a wide range of specific substances, including opioids, cocaine, cannabis, and alcohol, which is largely independent from the familial aggregation of both alcoholism and antisocial personality disorder. There was also evidence of specificity of familial aggregation of the predominant drug of abuse. Elevation in risk of this magnitude places a family history of drug disorder as one of the most potent risk factors for the development of drug disorders. Results suggest that there may be risk factors that are specific to particular classes of drugs as well as risk factors that underlie substance disorders in general. Merikangas, K.R., Stolar, M., Stevens, D.E., Goulet, J., Presisig, M.A., Fenton, B., Zhang, H., O'Malley, S.S., Rounsaville, B.J. Familial Transmission of Substance Use Disorders. *Archives of General Psychiatry*, 55, pp. 973-979, 1998.

Children, Particularly Sons, of Opiate Addicts with Major Depression at Increased Risk for Conduct Disorder and Global, Social, and Intellectual Impairment

Children (N=114, age 6 to 17 years) of 69 white methadone maintenance patients with (N=30) and without (N=39) major depression were evaluated for DSM-III-R diagnoses by the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic version and best estimate, and by measures of functioning (Children's Global Assessment Scale, Social Adjustment Inventory for Children and Adolescents, WISC, and Peabody Picture Vocabulary Test), and compared with children of historical controls without substance abuse history. Sons of opiate addicts with major depression were at increased risk for conduct disorder and global, social, and intellectual impairment compared with sons of opiate addicts without major depression and/or sons of controls with neither drug dependence nor depression. Sons of opiate addicts without major depression differed little from controls. Daughters of opiate addicts did not differ from controls in rates of disorders but had poorer social adjustment and nonverbal intelligence. Treatment settings such as methadone maintenance might afford an opportunity for primary and secondary prevention, both through early detection of childhood disorders and treatment of parental drug dependence and psychopathology. Nunes, E.V., Weissman, M.M., Goldstein, R.B., McAvay, G., Seracini, A.M., Verdeli, H., Wickramaratne, P.J. Psychopathology in Children of Parents with Opiate Dependence and/or Major Depression. *Journal of the American Academy of Child and Adolescent Psychiatry*, 37(11), pp. 1142-1151, 1998.

Ethnic Identity Is Mediated by Family Factors In Protecting Against Drug Use

This study examined the multiple components of ethnic identity, the place of this ethnic identity set in the mediational model of the path to drug use predicted by a family interactional framework, and the protective role of each component of ethnic identity. The participants were 259 male and 368 female African Americans in late adolescence. They responded to a structured questionnaire in individual interviews. Few of the specific components of ethnic identity were significantly related as main effects to drug use, and most of the effect of ethnic identity was mediated by the family set of variables. Each of the components of ethnic identity offset risks or enhanced protective factors from the ecology, family, personality, and peer domains, thereby lessening drug use. This pattern highlights the importance of incorporating ethnic identity into drug prevention programs which serve African-American youth. Brook, J.S., Balka, E.B., Brook, D.W., et al. Drug Use Among African Americans: Ethnic Identity as a Protective Factor. *Psychol Rep*, 83(3 Pt 2): pp. 1427-1446, 1998.

Young Adult Drug Use May Be Reduced by Early Interventions, Stronger Parent-Child Bonds

This study examined young adult drug use stemming from childhood aggression, the parent-child mutual attachment relationship, and the effect of unconventional behavior. Youngsters and their mothers were interviewed when the youngsters were early adolescents, late adolescents, and young adults. Additional data were collected from the mothers when their youngsters were children. The analysis was conducted on youngsters who had complete data at all 4 points in time. The findings were in accord with the family interactional model; that is, the parent-child mutual attachment relationship affects unconventional behavior in the youngster, which, in turn, affects young adult drug use. The results indicate that the parent-child mutual attachment relationship does so through the stability of: (a) the attachment relationship from childhood to young adulthood, (b) unconventional personality and behavioral attributes from early adolescence to young adulthood, and (c) drug use from early adolescence to young adulthood. The findings imply that early intervention with respect to aggression, interventions that focus on strengthening the parent-child bond and conventional behavior, and interventions aimed at early drug use should be most effective in reducing young adult drug use. Brook, J.S., Whiteman, M., Finch, S., and Cohen, P. Mutual Attachment, Personality, and Drug Use:

Pathways from Childhood to Young Adulthood. *Gen Soc Gen Psy Monogr*, 124(4), pp. 492-510, 1998.

Drug Use Among School Dropouts Is Influenced by Association With Drug Using Peers

A sample of 910 Mexican-American and white non-Hispanic school dropouts were surveyed regarding their alcohol, marijuana, and other drugs, and socialization characteristics that have previously been shown to be predictive of adolescent substance use. A structural equation model based on peer cluster theory was evaluated for goodness of fit and for differences in model characteristics by ethnicity and gender. Results partially confirmed peer cluster theory among school dropouts in that association with drug-using peers was the most powerful direct predictor of substance use. The effects of other socializing influences were indirect, mediated through association with drug-using peers. Some differences were present between Mexican-American and white non-Hispanic subgroups. Results were similar to those obtained from previous tests of this model among youth who remain in school, suggesting that social influences on drug use are similar across students and school dropouts. Association with drug-using peers dominates the prediction of substance abuse among school dropouts. Family communication of drug use sanctions helps to both limit substance use and strengthen family bonds. Prior school adjustment is likely to be an important protective factor limiting substance use among Mexican-American dropouts. Swaim, R.C., Bates, M.S., and Chevez, E. Structural Equation Socialization Model of Substance Use Among Mexican-American and White Non-Hispanic School Dropouts. *J Adolesc Health*, 23, pp. 128-138, 1998.

Effects of Drug Testing High School Athletes

Data from numerous studies have shown that high school athletes initiate hazardous drug use behaviors at rates similar to non-athletic peers, with the added risk of anabolic steroids and other ergogenic drug use. Some investigators have found higher use of alcohol and other high risk behaviors among those engaged in aggressive contact sports. Currently, schools from many states have initiated drug testing of adolescent athletes using urinalysis. The use of drug surveillance as a deterrent was upheld by the US Supreme Court in 1995 and 1998. However, the acceptability of the technique and its impact on future drug use by adolescents have never been studied. To assess the use of alcohol and other drugs in athletes, (n=1506) male high school football players and adolescent females (n=2085) were surveyed. Results included lifetime use of alcohol (76.2% male, 65.3% female), marijuana (29.4% male, 14.8% female) and amphetamines (8.4% male, 7.8% female). Participants were also surveyed by confidential questionnaire (1299 students from 28 high schools) to determine potential deterrent effects and acceptability of drug testing. Of those surveyed, only a small minority (<9%) said they would use drugs or alcohol (12%) if random drug testing were school policy. Importantly, drug testing received broad student support. Goldberg, L., Elliot, D., Moe, E., Kuehl, K., and Clarke, G. Acceptability and Potential Deterrent Effects of Drug Testing. *Medicine and Science in Sports and Exercise*, 31(5)S, 1999. Gender Differences in Use of Prescribed Psychotropic Drugs Data from the 1989 National Ambulatory Medical Care Survey (NAMCS) was used to examine gender differences in aggregate psychotropic drug use and use of specific therapeutic categories--anxiolytics, sedative-hypnotics, antidepressants, and antipsychotics. Logistic regression analysis was used to estimate the probability of psychotropic drug use in aggregate. For equations where gender was statistically significant, separate logistic regression equations were estimated to determine the explanatory variables that vary by gender. The probability of receiving any psychotropic drug is 55% greater in office visits by women than by men, all else constant. Further, gender is a positive and significant predictor of anxiolytic and antidepressant use. Variables estimating anxiolytic and antidepressant use that differ by gender include diagnosis, physician specialty, and payment source for the office visit. Findings confirm research that has demonstrated that women are more likely than men to receive anxiolytics and antidepressants in office-based care. In addition, there were significant differences in the predictors of drug use for women and men. Simoni-Wastila, L. Gender and Psychotropic Drug Use. *Medical Care* 36(1), pp. 88-94, 1998.

Clusters Of Marijuana Use In The United States

To assess the extent of clustering of marijuana use within United States neighborhoods, researchers at Johns Hopkins University analyzed data from the annual National Household Survey on Drug Abuse conducted during the period 1990-1995 using alternating logistic regression, a recently developed statistical method. Estimates of pairwise odds ratios ranged from 1.3 (95% confidence interval 1.22-1.42) for the lifetime history of marijuana use to 2.0 (95% confidence interval 1.6-2.6) for recent sharing of marijuana from one person to another. This is approximately the same order of magnitude as the clustering of diarrheal disease in villages of the less developed nations of the world. The extent of clustering of marijuana use was not very dependent upon either neighborhood-level or individual-level characteristics measured in the survey (e.g., age, sex, race, income levels). The more recent and intensive the

marijuana use, the greater the clustering within neighborhoods. In addition, the practice of sharing marijuana with other persons also occurs in clusters within neighborhoods. This sharing may be one of the fundamental interpersonal and social processes that accounts for clustering of marijuana use; it is a potential target for future community- and school-oriented prevention programs to curb the increasing prevalence of youthful marijuana use. Bobashev, G.V., and Anthony, J.C. *American Journal of Epidemiology*, 148(12), pp. 1168-1174, Dec. 1998.

Substance Abuse And Associated Psychosocial Problems Among Argentina Adolescents: Sex Heterogeneity And Familial Transmission

Researchers from the University of Pittsburgh collaborated with researchers in Argentina on a study to clarify the effects of sex and familial transmission in the psychosocial concomitants of substance abuse problems among adolescents. Male (N=956) and female (N=303) adolescents in school, and male adolescents in a drug treatment program (N=51) in Buenos Aires Province, Argentina were administered a translated version of the Drug Use Screening Inventory. Use of substances, familial substance abuse and associations between psychosocial problem domains and substance abuse problems were examined. Substance abuse and psychosocial problems varied broadly by sex. Female adolescents in the school-based sample were found to generally report higher levels of psychosocial problems and greater use of minor tranquilizers than school boys or boys in treatment for substance abuse. Conduct deviancy was associated with substance abuse problems only in males, while health problems were associated only in females. However, among all youth, substance abuse problems were found to be associated with older age, greater social competency, problems in school performance, and involvement with deviant peers. Familial substance abuse was associated with substance abuse problems among all adolescents, but the pattern of associations with other psychosocial problems differed between males and females. Heterogeneity in socioeconomic status was found in the associations between psychosocial problems, adolescent substance abuse, and familial substance abuse. The results are consistent with a syndrome of problem behaviors and demonstrate the cross-cultural consistency of sex heterogeneity in adolescent substance abuse and its consequences. Moss, H.B., Bonicatto, S., Kirisci, L., Girardelli, A.M., Murrelle, L. *Drug and Alcohol Dependence* 52(3), pp. 221-230, 1998.

Executive Cognitive Functioning, Temperament, and Antisocial Behavior in Conduct-Disordered Adolescent Females

Investigators from CEDAR assessed whether low executive cognitive functioning (ECF) and a difficult temperament are related to aggressive and nonaggressive forms of antisocial behavior (ASB) in 249, 14-18-year-old, conduct-disordered females and controls. ECF was measured using neuropsychological tests; temperament was measured using the Dimensions of Temperament Survey--Revised; and ASB was assessed using psychiatric symptom counts for conduct disorder. The conduct-disordered females exhibited lower ECF capacity and greater difficult temperament compared with controls. The combined influence of low ECF and difficult temperament was significantly related to both forms of ASB. In comparison with low ECF, difficult temperament was more strongly related to nonaggressive ASB, whereas in comparison with difficult temperament, low ECF was more strongly related to aggressive ASB. Last, ECF mediated the relation between difficult temperament and aggressive ASB. Giancola, P.R., Mezzich, A.C., and Tarter, R.E. *Journal of Abnormal Psychology*. 107(4), pp. 629-641, Nov 1998.

Comorbidity of Alcoholism with Anxiety and Depressive Disorders in Four Geographic Communities

The comorbidity of alcoholism with anxiety and depressive disorders was examined in four epidemiologic investigations from diverse geographic sites. Despite variability in lifetime prevalence rates for these disorders, a strong cross-site consistency in magnitude and specific patterns of comorbidity existed. Individuals with alcohol abuse or dependence generally experienced a two- to threefold increased risk of anxiety and depressive disorders. Phobic conditions typically preceded the onset of alcoholism, but no systematic pattern was observed for panic or depressive disorders. Considerable heterogeneity was observed concerning the impact of comorbid conditions on symptoms of the index disorder. While the presence of comorbid anxiety or depressive disorders was consistently associated with moderate increase in the symptoms of alcohol abuse or dependence, alcoholism was associated with large increases in the number of depressive symptoms and little or no increase in phobic symptoms. Findings are discussed in terms of the self-medication hypothesis and the etiologic heterogeneity of these forms of comorbidity in the general population. Swendsen, J.D., Merikangas, K.R., Canino, G.J., Kessler, R.C., Rubio-Stipec, M., and Angst, J. *The Comorbidity of Alcoholism with Anxiety and Depressive Disorders in Four Geographic Communities. Comprehensive Psychiatry* 39, 4, pp. 176-184, (July/August), 1998.

Co-morbidity between Panic Disorder and Alcoholism May Not Be a Consequence of Self-medication of Panic Symptoms

This study examines the patterns of familial aggregation and co-morbidity of alcoholism and anxiety disorders in the relatives of 165 probands selected for alcoholism and/or anxiety disorders compared to those of 61 unaffected controls. Probands were either selected from treatment settings or at random from the community. DSM-III-R diagnoses were obtained for all probands and their 1,053 first-degree relatives, based on direct interview or family history information. Findings indicate (1) alcoholism was associated with anxiety disorders in the relatives, particularly among females; (2) both alcoholism and anxiety disorders were highly familial; (3) familial aggregation of alcoholism was attributable to alcohol dependence rather than to alcohol abuse, particularly among male relatives; and (4) the pattern of co-aggregation of alcohol dependence and anxiety disorders in families differed according to the subtype of anxiety disorder; there was evidence of a partly shared diathesis underlying panic and alcoholism whereas social phobia and alcoholism tended to aggregate independently. The finding that the onset of social phobia tended to precede that of alcoholism, when taken together with the independence of familial aggregation of social phobia and alcoholism, supports a self-medication hypothesis for the co-occurrence of social phobia and alcoholism. In contrast, the lack of a systematic pattern in the order of onset of panic and alcoholism among subjects with both disorders as well as evidence for shared underlying familial risk factors suggest that co-morbidity between panic disorder and alcoholism is not a consequence of self-medication of panic symptoms. The study emphasizes the importance of examining co-morbid disorders and subtypes thereof in identifying sources of heterogeneity in the pathogenesis of alcoholism. Merikangas, K.R., Stevens, D.E., Fenton, B., Stolar, F.M., O'Malley, S., Woods, S.W., and Risch, N. Co-morbidity and Familial Aggregation of Alcoholism and Anxiety Disorders. *Psychological Medicine* 28, pp. 773-788, 1998.

Cigarette Use Increases Following Drug Abuse Treatment

To test the hypothesis that participation in drug treatment and risk-behavior bias predict greater cigarette use, researchers at UCLA analyzed data from a 3-wave survey of 346 drug abusers to assess the influence of risk-behavior bias, drug use, prior cigarette use, and prior and current participation in drug treatment on subsequent cigarette use. After controlling for prior levels of cigarette use with a longitudinal path model, it was found that participation in drug treatment at Wave 2 significantly predicted increased cigarette use at Wave 2. There were similar results at Wave 3. Additional analyses indicated that reduced heroin use was especially associated with more smoking. Risk-behavior bias predicted more drug and cigarette use and predicted less participation in drug treatment at Wave 3. These results suggest that drug treatment, reduced heroin use, and a tendency toward risky behavior may lead to increased cigarette use, which may represent a form of substance replacement. Conner, B.T., Stein, J.A., Longshore, D., and Stacy, A.W. Associations Between Drug Abuse Treatment and Cigarette Use: Evidence of Substance Replacement. *Experimental and Clinical Psychopharmacology* 7, pp. 64-71, 1999.

The Etiology of Adult and Adolescent Substance Use May Differ--Substance Use Patterns in Milwaukee Gangs

A study of the patterns of substance use by male and female gang members in Milwaukee, Wisconsin, from their teenage years in the 1980s into adulthood indicate that the gangs started out as one form of neighborhood-based drug-using peer groups. Variation existed in drug use but family variables explained little of the variation. Male gang members raised in families with a history of gang involvement and drug use were more likely than other gang members to use cocaine and to use it seriously. On the other hand, severe family distress was not related to onset, duration, nor seriousness of cocaine use in either males or females. Cocaine use for both males and females increased in adulthood. It appears that the etiology of adult and adolescent drug use may differ. Neither social control theory nor differential association theory is well suited to explain the variations in gang drug use by age or gender. Hagedorn, J.M., Torres, J., and Giglio, G. Cocaine, Kicks, and Strain: Patterns of Substance Use in Milwaukee Gangs. *Contemporary Drug Problems* 25, Spring, pp. 113-145, 1998.

Characteristics of Inconsistent Respondents Who Have "Ever Used" Drugs in a School-Based Sample

Inconsistency of reporting of lifetime drug use has been recognized in numerous longitudinal surveys, and some researchers have coined the term "recanting" to describe denial of ever-use at follow-up when use has been acknowledged at an earlier contact. Investigators at the University of Illinois at Chicago examined the predictors of inconsistent responses from adolescents to questions about whether they ever used alcohol, cigarettes, and marijuana. Male adolescents had significantly higher rates of inconsistent responses than female adolescents. Black and Hispanic adolescents had significantly higher rates of inconsistent responses regarding ever using alcohol and cigarettes (only for Black) than White adolescents. The subjects' living status and academic achievements were significant predictors of inconsistent responses regarding ever using marijuana. Thus, these results are consistent with the notion that inconsistent responses may bias the estimation of the prevalence of ever using drugs in multivariate analyses. Siddiqui, O., Mott, J.A., Anderson, T.L., and Flay, B.R. Measurements, Instruments, Scales, and Tests -- Characteristics of Inconsistent Respondents who have "Ever Used" Drugs in a School-Based Sample. *Substance Use & Misuse*, 34(2), pp. 269-295, 1999.

Stressful Life Events and Adolescent Substance Use and Depression: Conditional and Gender Differentiated Effects

Stressful life circumstances have myriad influences on human health and behavior. Early research focused on the variable distribution of stress and its effects by socioeconomic status, race, and gender. More recent research indicates that variation by age is also an important consideration. For example, adolescent reactions to stressful life events are often inconsistent with adult reactions to similar life situations and transitions. Moreover, since most studies assess only a single outcome-usually depression-they risk classification bias since analyses exclude other potential stress-related outcomes. This paper assesses the gender distinct effects of stressful life events on two outcomes among adolescents, substance use and depressive symptoms. The results of a second-order regression model indicate that life events affect female, but not male, depressive symptoms, especially when self-esteem is low or mastery is high. Furthermore, life events affect substance use when peer drug use is high, or when parental support is low, but this latter effect is limited to female adolescents. Hoffmann, J.P., and Su, S.S. *Substance Use & Misuse* 33(11), pp. 2219-2262, 1998.

Prevalence of Homelessness Among Adolescents in the United States

Homeless adolescents represent one of the nation's most vulnerable groups and are believed to be at high risk for drug abuse. This study, conducted by investigators at Research Triangle Institute, reports the 12-month prevalence of homeless episodes among US adolescents. Interviews were conducted in 1992 and 1993 with a representative household sample of 6496 adolescents aged 12 to 17 as part of the Youth Risk Behavior Survey sponsored by the Centers for Disease Control and Prevention. Respondents reported whether they had spent the night in any of a variety of locations other than home during the previous 12 months. Findings indicate 7.6% of the youths questioned reported that they had spent at least 1 night in a youth or adult shelter (3.3%), public place (2.2%), an abandoned building (1.0%), outside (2.2%), underground (0.4%) or with a stranger (1.1%). Boys were much more likely than girls to report having experienced a homeless episode. This study suggests that homelessness among adolescents is not simply an urban problem and that prevention programs targeting homeless youth should be implemented nationwide. Ringwalt, C., Greene, J., Robertson, M., McPheeters, M. *American Journal of Public Health*, 88(9), pp. 1325-1329, 1998.

Major Depression in Children of Parents Dependent on Opiates is Associated with Increased Risk of Physical Health Problems

A study to examine the strength and specificity of the association between depression and physical health problems in children and adolescents whose parents were dependent upon opiates found the offspring to be at increased risk of physical health problems. The sample consisted of offspring ages 6-17 (mean age 11 years) of opiate addicts who had a history of MDD (N=28); other mood disorders (N=31); no history of mood disorders but other psychiatric disorders (N=92); or no history of psychiatric disorder (N=127). Detailed psychiatric assessment and medical history of the offspring by direct interview with the offspring and an informant were obtained blind to parental diagnosis. After controlling for possible confounders, there was an increased risk of dermatological disorders, headache, other neurological/neuromuscular disorders, bronchitis, other respiratory disorders and hospitalizations for nonsurgical procedures in offspring with MDD, as compared to nonpsychiatrically ill controls. The offspring with other mood disorders had a slightly elevated risk. Major depression in children and adolescents whose parents are dependent on opiates is associated with increased risk of physical health problems. This is consistent with other reports; however,

the timing of the physical health problems requires further study. McAvay, G.M., Nunes, E.V., Zaider, T.I., Goldstein, R.B., Weissman, M.M. Physical Health Problems in Depressed and Non Depressed Children and Adolescents of Parents with Opiate Dependence. *Depression and Anxiety*, 9, 1999.

Startle Response May Be Vulnerability Marker to Discriminate among Children at Risk for Development of Anxiety Disorders and/or Alcoholism

This study examined startle reflex as a possible vulnerability marker among offspring of parents with anxiety disorders and/or alcoholism. Subjects were male and female offspring (N=66), 10 to 17 years of age, of probands who participated in a family study of comorbidity of alcoholism and anxiety disorders. Testing consisted of examining the startle reflex and its modulation by prepulse stimuli (prepulse facilitation and prepulse inhibition). Different components of the startle discriminated among children of parents with anxiety disorders and/or alcoholism, and children of normal controls. Specifically, startle magnitude was elevated in children with a parental history of an anxiety disorder whereas startle habituation and prepulse inhibition were impaired in children with a parental history of alcoholism. Findings suggest that individual differences in startle reflex may serve as a vulnerability marker for the development of anxiety disorders and alcohol problems. Grillon, C., Dierker, L., and Merikangas, K.R. Fear-Potentiated Startle in Adolescent Offspring of Parents with Anxiety Disorders. *Biological Psychiatry*, 44, pp. 990-997, 1998.

Sequence of Powder Cocaine and Crack Use among Arrestees in Los Angeles County

While the extent of cocaine use, characteristics of users, and consequences of dependence are well documented for both powder cocaine and crack, few studies have dealt with the sequence or progression of use between the two forms of cocaine. Drawing on arrest data from county jails in Los Angeles, investigators at UCLA identified four sequences of powder cocaine and crack use and examined each sequence in terms of user characteristics, history of use, dependence, contact with the criminal justice system, and concomitant use of other drugs. Findings indicate that (1) arrestees who initiated cocaine use with the powder form of the substance are more likely to progress to using crack than to restrict their use of cocaine to powder; (2) crack-initiated users tend more often to use crack only than to progress to powder cocaine; (3) when used interchangeably, powder cocaine and crack can interact and reinforce each other, resulting in a higher level of use and dependence on both forms of the substance. Shaw, V.N., Hser, Y.I., Anglin, M.D., and Boyle, K. *American Journal of Drug and Alcohol Abuse*, 25(1), pp. 47-66, 1999.

Ethnic and Gender Differences in Drug Use and Resistance

A survey was conducted to measure drug use, drug offers and drug resistance and to compare male and female members of different ethnic groups in seventh grade classes in the Phoenix metropolitan area. The survey was administered to over 4,000 students, with usable data obtained from 3,080. Significant ethnic and gender differences were described in drug use and, more importantly, in the drug offer and resistance process. Results indicate younger adolescents (12-13) do not possess large or sophisticated repertoires of strategies to resist drug offers and most offers come from acquaintances while previous studies report offers come from more intimate relationships for older adolescents. Also illustrated was that ethnicity and gender are related to drug use and how drugs are offered and resisted. This suggests that ethnic and gender specific approaches are needed in prevention curricula and refusal and life skills should be stressed. Moon, D.G., Hecht, M.L., Jackson, K.M., & Spellers, R. Ethnic and Gender Differences and Similarities in Adolescent Drug Use and the Drug Resistance Process. *Substance Use and Misuse*, 34, pp. 1059-1083, 1999.

Females At-Risk for Anabolic Steroid Use

Three national surveys document an increasing prevalence of young women's anabolic steroid (AS) use. Both local survey and national data indicate prevalences of AS use among young women of approximately 1%. Predictors of AS use and the relationship to disordered eating behavior (DEB) have not been defined. This study surveyed 2,090 middle and high school-aged females using a 140-item questionnaire. Tendency toward DEB and physique-altering drug use (including AS) and potential risk factors in the domains of knowledge, beliefs, psychological factors, peer/environmental effects, demographics, drug use, and deviant behaviors were assessed. One-hundred and eleven (5.3%) subjects indicated a high intent for future AS use. Of those at high risk for DEB (24% total), 12% also were at risk for AS use. Those at risk for both DEB and AS use also indicated greater use of supplements, cocaine, alcohol

and diet pills ($p < 0.005$ for each). They also exhibited less belief in AS adverse effects, greater perceived peer AS use, and more sexual partners ($p < 0.005$ for each). Those at risk for DEB, were also at risk and exhibited more deviant behavior. Because similar predictors are present for DEB and AS use, programs designed to prevent DEB also should address AS use. Elliot, D.L., Moe, E.L., Duncan, T., and Goldberg, L. Who Are the Young Women at Risk for Anabolic Steroid Use? *Medicine and Science in Sports and Exercise*, 31(5)S, 1999.

Frequency of Cigarette Use by 7th Graders is a Strong Predictor of Dropping Out of High School

This study examines the impact of early adolescent drug use on subsequent school drop out in a sample of 4,390 adolescents from California and Oregon. Participants were initially surveyed in the 7th grade and again six years later when they should have completed 12th grade. Controlling for demographics, family structure, academic orientation, early deviance, and school environment, logistic regression analyses showed that frequency of cigarette use during 7th grade predicted dropping out of high school. Separate analyses by race/ethnicity replicated this finding for Asians, Blacks, and Whites, but not for Latinos. For Latinos, early marijuana use predicted dropping out. The results suggest that preventing or reducing the incidence of early smoking and marijuana use may help reduce the probability of dropping out of high school. Ellickson, P., Khanh B., Bell, R. and McGuigan, K. Does Early Drug Use Increase the Risk of Dropping Out of High School? *Journal of Drug Issues*, 28(2), 1998.

Parental Monitoring

The link between parental monitoring and child problem behavior has been established in three areas: substance abuse, anti-social behavior, and safety and injury. This paper reviews the work to date on the construct and accomplishes three goals: first, to provide an empirical rationale for placing parental monitoring of children's activities as a key construct in development and prevention research; second, to stimulate more research on parental monitoring and provide an integrative framework for various research traditions as well as developmental periods of interest; third, to discuss current methodological issues that are developmentally and culturally sensitive and based on sound measurement. Possible intervention and prevention strategies that specifically target parental monitoring are discussed. Dishion, T.J., and McMahon, R.J. Parental Monitoring and the Prevention of Child and Adolescent Problem Behavior: A Conceptual and Empirical Formulation. *Clinical Child and Family Psychology Review*, 1, pp. 61-75, 1998.

Antecedents of Substance Use Initiation

Initiation of substance use before the age of 15-16 is a distinct risk factor for a variety of mental health problems and eventual drug abuse. Using multi-method, multi-agent measures of child, family, and peer antecedents at age 9-10, the investigators studied the longitudinal effects in an at-risk sample of 206 boys. Event history analysis was used to examine the antecedents to patterned alcohol and tobacco use, and experimentation with marijuana between age 11-16. Univariate models revealed that at Grade 4, most constructs were prognostic of boys' early substance use. Multivariate event history models clarified the risk and protective structure associated with tobacco, alcohol and marijuana use. The effects of family context, family management and peer factors were entirely mediated through characteristics of the boys at Grade 4 for alcohol initiation. Anti-social behavior was key for early onset alcohol and marijuana use. Low SES and low sociometric status were predictive of early tobacco use. Interaction effects for prediction of marijuana and tobacco onset indicated that their association with family management and boy's characteristics may vary by level of parental substance use. Dishion, T.J., Capaldi, D.M., and Yoerger, K. Middle Childhood Antecedents to Progression in Male Adolescent Substance Use: An Ecological Analysis of Risk and Protection. *Journal of Adolescent Research*, 14(2), pp. 175-206, 1999.

Sexual and Physical Abuse at Home Predicts Suicide Attempts by Homeless Street Youth

A study was conducted to examine the relationship between home life risk factors and suicide attempts among homeless and runaway street youth recruited from both shelters and street locations in Denver, New York City, and San Francisco. Street youth (N=775) age 12-19 years old were recruited in 1992 and 1993 by street outreach staff for interview. Cross-sectional, retrospective data were analyzed to examine the relationship between suicide attempts and antecedent home life variables. Suicide attempts were reported by 48% of the females and 27% of the males, with a mean of 6.2 times for females and 5.1 times for males. Among the females, 70% reported sexual abuse and 35% reported physical abuse; among males, 24% reported sexual abuse and 35% reported physical abuse. Sexual

and physical abuse before leaving home were independent predictors of suicide attempts for both females and males. Among street youth in this study who were sexually or physically abused, the odds of attempting suicide were 1.9 to 4.3 times the odds of attempting suicide among those not sexually or physically abused. Interventions attempting to reduce risk behaviors in this population must include assessments of suicidal behaviors as well as components for assisting youth in dealing with the behavioral and emotional sequelae of sexual and physical abuse. Molnar, B.E., Shade, S.B., Kral, A., et al. Suicidal Behavior and Sexual/Physical Abuse Among Street Youth. *Child Abuse and Neglect*, 22 (3): pp. 213-222, 1998.

Tobacco Use and Perception of Harm Among Mexican American Youth

This study sought to understand reasons for an increase in smoking and tobacco-related diseases among the Hispanic population. It examined the relationship between gender, level of cultural identification, migrant status, and grade level and tobacco use and perception of harm among Mexican American youth. Males were more likely to use tobacco than females when grade, cultural identification, and migrant status of parents are held constant. No gender effect was found for lifetime cigarette use. The odds of using cigarettes and smokeless tobacco increased substantially across grades. Effects were found for Mexican American/Spanish and Anglo/White American cultural identification and daily cigarette use. Youths who belonged to nonmigrant families or who identified with a traditional Mexican American or Spanish culture were more likely to consider regular tobacco use as harmful. These and other findings have implications for preventing future use of tobacco among Mexican American youth. Casas, J.M., Bimbela, A., Corral, C.V., et al. Cigarette and Smokeless Tobacco Among Migrant and Nonmigrant Mexican American Youth. *Hispanic J Behavioral Sciences*, 22 (1), pp. 102-121, 1998.

Underreports of Drug Use More Likely in STD Patients Compared to Arrestees at Jail Sites

This paper examines the validity of self-report of drug use in several important high-risk samples by comparing survey answers with urinalysis results. The analyses include data obtained from face-to-face interviews with 1536 patients in sexually transmitted disease (STD) clinics, 1564 patients in hospital emergency rooms (ERs), and 2034 recent arrestees in jails. Using urinalysis as the criterion measure, considerable underreporting was observed, particularly among STD and ER subjects using cocaine and opiates. A logistic regression analysis on factors related to the underreporting was conducted for both cocaine and opiates. The results showed that a lower degree of underreporting was associated with subjects at jail sites (compared to STD subjects) and those who self-reported lifetime drug dependence. Hser, Y.I., Maglione, M., and Boyle, K. Validity of Self-Report of Drug Use Among STD Patients, ER Patients, and Arrestees. *Am J Drug Alcohol Abuse*, 25(1), pp. 81-91, 1999.

Prevention of Drug Use in Adolescent Athletes

To test the ATLAS (Adolescents Training and Learning to Avoid Steroids) program to reduce anabolic steroids (AS) and alcohol and other drugs among adolescent athletes, 31 football teams (n=3207) were assessed in a randomized controlled study. Three successive annual cohorts were entered (1994-1996). Classroom curriculum and exercise training sessions were delivered by peer leaders, facilitated by coaches and strength trainers. The program included sports nutrition and strength training, AS risks and benefits, effects of AS use in sports, drug refusal role play, and creating anti-steroid and health promotion messages. Questionnaires assessing AS use, potential risk and protective factors, and AOD use were administered before and after the intervention and up to one year later. All cohorts were combined for season's end findings and the first 2 cohorts are combined for the 1-year follow-up. At season's end, AS use was more than 50% lower among experimental subjects ($p=0.035$), with borderline level of significance at 1-year ($p=0.072$). When alcohol and the illicit drug use index (marijuana, amphetamines and narcotics) was assessed, experimental students used fewer drugs ($p=0.041$). Other long-term intervention effects included fewer students reporting drinking and driving ($p=0.004$), lower supplement use ($p=0.009$), and better nutrition ($p=0.015$). Moe, E., Goldberg, L., Elliot, D., MacKinnon, D., and Cheong, J. Reducing Drug Use and Promoting Healthy Behaviors Among Athletes: the ATLAS Program. *Medicine and Science in Sports and Exercise*, 31(5)S, 1999.

Pregnancy Among Three National Samples of Runaway and Homeless Youth

Investigators at Research Triangle Institute compared estimates of the prevalence of pregnancy among runaway and homeless youth between the ages of 14 and 17 years in various settings with each other and with youth in the general population. Comparisons used three surveys of youth: (1) the first nationally representative survey of

runaway and homeless youth residing in federally and non-federally funded shelter, (2) a multi-city survey of street youth, and (3) a nationally representative household survey of youth with and without recent runaway and homeless experiences. Youth living on the streets had the highest lifetime rates of pregnancy (48%), followed by youth residing in shelters (33%) and household youth (<10%). The investigators concluded that shelter and street youth were at much greater risk of having ever been pregnant than were youth in households regardless of whether they had recent runaway or homeless experiences. Such youth need comprehensive services, including pregnancy prevention, family planning, and prenatal and parenting services. Greene, J., and Ringwalt, C. *Journal of Adolescent Health*, 23(6), pp. 370-377, 1998.

The Female Atlanta Study (FAST): Crack Cocaine and Women

Dr. Claire Sterk explores the lives of 259 female drug users based on participant observation, close-ended interviewing, open-ended, in-depth interviewing, ethnographic mapping, and community consultants. In addition to drug copping zones in which drug selling and using were visible, women were recruited in neighborhoods in which drug use was just as prevalent but hidden. The book moves through the woman's initial drug use experimentation, controlled use, and evolution to current regular use. The various patterns of crack cocaine use and income-generating activities are organized into a typology: women who finance their use through involvement in the drug business, through illegal activities other than prostitution, through prostitution including sex for crack exchanges, and women who did not use drugs until they were in their thirties or older as they struggled to survive. Overall, the women's steady relationships with drug users were more mutually rewarding than relationships with non-users. Frequently, the women believed pregnant women should eliminate or reduce drug use; however, many women failed to learn of their pregnancy until the second trimester or later. Once aware of their pregnancy, several women shifted from smoking crack cocaine to drinking alcohol, assuming a legal substance was safer. Criminalization of drug use by pregnant women reduced their seeking prenatal care. Once pregnant, some chose abortion or drug-induced miscarriage; some elected adoption; others chose to become mothers. Many of the women had at least one experience with drug treatment and described motivators and barriers to drug treatment. The majority of the women had heard of HIV/AIDS, but many were misinformed about risk behaviors and risk reduction. Their claims to have made behavioral changes to reduce risk often referred to intentions. Among the women tested, very few felt prepared for the waiting period between test and results. At times, women increased their HIV risk-taking during this waiting period. The women who tested negative for HIV still led lives impacted by the HIV epidemic. They faced a continual challenge to remain HIV negative, basing their actions on the assumption that they or their partner was infected with HIV. Violent encounters were common--childhood and adult--and linked violence to HIV risk-taking. The women's perceptions of the past, present, their aspirations, and impact of the constantly changing drug market on their lives is interlaced with their acknowledgement that societal changes were needed to reduce racism, poverty, and sexism but they also described actions they could take themselves. Sterk, C.E. *Fast Lives: Women Who Use Crack Cocaine*. Philadelphia: Temple University Press, 1999.

A Test of the Social Development Model

The social development model (SDM) is a general theory of human behavior that hypothesizes that similar developmental processes can lead to either prosocial or antisocial outcomes. The current study examines the relation between family behavior and early anti-social behavior using data on 938 first and second grade students in ten suburban public elementary schools. Children were part of the longitudinal Raising Healthy Children project, which began in 1993. Child, teacher and parent reports were collected annually in the spring from 1994 through 1996. Analysis one examined the prosocial path of the SDM. The model fit well, explaining 25% of the variance in early antisocial behavior. However, the path between skills and rewards from the family was not significant. A better fit was obtained when the model included paths from skills to beliefs and skills to antisocial behavior. In analysis two, the sample was split into two groups, those whose parents modeled problem behavior (heavy drinking, illicit drug use and domestic violence) and those who did not. Two differences emerged between the two groups. First, the strength of the path between skills and problem behavior was significantly stronger for children whose parents modeled problem behaviors. Second, the belief in family values path to antisocial behavior was not significant for children whose parents modeled problem behaviors. Thus, beliefs provide a significant protective effect for children whose parents do not model problem behaviors, but not for children in families where parents model problem behaviors. Catalano, R.F., Oxford, M., Harachi, T.W., Abbott, R. D., Haggerty, K.P. *Modeling the Development of Early Antisocial Behavior: A Test of the Social Development Model to Predict Problem Behavior during the During the Elementary School Period*. *Criminal Behavior and Mental Health*, 9, pp. 40-57, 1999.

Program Evaluation for Family-based Interventions

This article illustrates a program evaluation approach for the study of family intervention outcomes in general populations. Thirty-three rural schools were randomly assigned to 1 of 3 conditions: The Preparing for the Drug Free Years program (PDFY), the Iowa Strengthening Families Program (ISFP), and a minimal-contact control group. Self-report and observational data collected from 523 families were used to develop measurement models of 3 latent parenting constructs that included measurement method effects. Analyses were conducted to ensure initial and attritional-related group equivalencies and to assess school effects. Structural equation models of the hypothesized sequence of direct and indirect effects for both PDFY and ISFP were then fit to the data. All hypothesized effects were significant for both interventions. Spoth, R., Redmond, C., Shin, C. Direct and Indirect Latent-variable Parenting Outcomes of Two Universal Family-focused Preventive Interventions: Extending a Public Health-oriented Research Base. *Journal of Consulting and Clinical Psychology*, 66(2), pp. 385-399, 1998.

Decreasing Drug Use in High-Risk Populations

Social-influence-based prevention programs can significantly delay the onset of tobacco, alcohol, and other drug use and slow the rate of increase in substance use prevalence among entire populations of early adolescents. Less is known about the capacity of these and other primary prevention programs to effect decreases in substance use. This is an important question since some youth have already begun to experiment with drugs by the time primary prevention programs are offered to them. In a 3.5-year follow-up of data from the Midwestern Prevention Project effects of a primary prevention program were found to decrease drug use among adolescents who were users at either sixth or seventh grade. This research suggests that social-influence-based primary prevention programs can have an impact on students who are users at baseline. The advantage of such a primary program is that it may reach and affect a "silent," not-yet-identified high-risk population of early drug users in a nonstigmatizing, nonlabeling fashion at an age when youth are more easily persuaded. Chou, P.C., et. al. Effects of a Community-Based Prevention Program on Decreasing Drug Use in High-Risk Adolescents. *American Journal of Public Health*, 88(6), June 1998.

A Longitudinal Perspective on Entitlement Income Among Homeless Adults

Researchers at the Alcohol Research Group of the Public Health Institute in Berkeley, California, examined sources of income in a sample of homeless adults to determine whether certain subgroups more consistently obtain entitlement income and are more likely to continue receiving it over time. From a baseline sample of 564 homeless residents of Alameda County, California, 397 were interviewed at both five-and 15-month follow-up intervals. Information was obtained on income received from public sources in the past 30 days before each interview, including general assistance, Aid to Families with Dependent Children (AFDC), Supplemental Security Income, or Social Security Disability Insurance. Data were also obtained on psychiatric diagnosis, race, marital status, education, duration of homelessness in adulthood, household status, and reported disability. At baseline, fewer than half of the respondents were receiving any entitlement income. The benefits of almost half of the AFDC and general assistance recipients were terminated during the 15-month period. Respondents who continued receiving entitlement income over the 15-month period were more likely to be black, to be women alone or with children, to have a family history of receiving welfare, and to report a disability. Respondents with dual disorders were six times more likely than others to have their benefits terminated. The investigators conclude that entitlement income is tenuous for many homeless adults, particularly those with dual diagnoses. Zlotnick, C., Robertson, M., and Lahiff, M. *Psychiatric Services*, 49(8), pp. 1039-1042, 1998.

Psychopathology Among Offspring of Parents with Substance Abuse and/or Anxiety Disorders

In a study with a high-risk population of children under age 18 of parents who served as probands in a family study of comorbidity of substance abuse and anxiety disorders, there was a strong degree of specificity of familial aggregation of both the anxiety disorders and substance use disorders. Rates of conduct disorder and depression were elevated among offspring of all affected parents. Inclusion of co-parent disorders in the evaluation of familial transmission in the present study strengthened the findings regarding the specificity of transmission of the anxiety disorders and the links between both parental substance abuse and antisocial personality with child conduct disorder. Merikangas, K.R., Dierker, L.C., and Szatmari, P. Psychopathology Among Offspring of Parents with Substance Abuse and/or Anxiety Disorders: A High-Risk Study. *Journal of Child Psychology and Psychiatry*, 39(5), pp. 711-720, 1998.

Relation between Intervention Efficacy and Cumulative Family Risk

Family risk-related variations in proximal parent and young adolescent outcomes of a universal family-focused preventive intervention were examined using a cumulative index of risk incorporating sociodemographic characteristics and social-emotional adjustment measures. Results of an initial investigation involving 209 families of young adolescents suggested that intervention efficacy was largely unrelated to cumulative family risk. These findings were replicated with a second sample of 428 families. Spoth et al., Risk Moderation of Parent and Child Outcomes in a Preventive Intervention: A Test and Replication. *American Journal of Orthopsychiatry*, 68(4), pp. 565-579, 1998.

Extracurricular Activities Related to School Retention Among Mexican Americans Students

With a growing Mexican American population and an increasing dropout rate predicted for this group, research is needed to examine ways of deterring this trend and increasing retention rates. The current study examined extracurricular activity, perception of school, and ethnic identification, and the association with school retention rates among Mexican American and White non-Hispanics. Individuals reporting participation in extracurricular activity were 2.30 times more likely to be enrolled in school than were those not participating in extracurricular activity. Mexican Americans reporting a higher White non-Hispanic ethnic identity level were 2.41 times more likely to be enrolled in school and had a more positive perception of school than did Mexican American individuals reporting low levels of White non-Hispanic ethnic identification. Davalos, D.B., Chavez, E.L., and Guardiola, R.J. The Effects of Extracurricular Activity, Ethnic Identification, and Perception of School on Student Dropout Rates. *Hispanic J Behavioral Sciences*, 21(1), pp. 61-77, 1999.

Assessing Change during Psychotherapy

This article provides an overview of methodological and conceptual issues underlying the assessment of change during psychotherapy with children and families. Three central considerations are discussed: (1) What changes do we measure? (2) When do we measure change? (3) How do we measure change? Measurement of change should be a priority of intervention research and is enhanced by: inclusion of multiple assessment points at theoretically important points during and after the intervention; use of reliable and valid measures of the change process; analysis of mediating, moderating, side effect, and clinical change variables; and protocols that assess dynamic rather than static constructs. Behaviors of interest should be measured in natural environments that are selected for their developmental relevance with regard to the age of the child and the problem behavior. Illustrations of key points are provided from the Adolescent Transitions Program, a theoretically based intervention program targeting high-risk youth. Eddy, J.M., Dishion, T.J., and Stoolmiller, M. The Analysis of Change in Children and Families: Methodological and Conceptual Issues Embedded in Intervention Studies. *Journal of Abnormal Child Psychology*, 26, pp. 53-69, 1998.

Comparative Perceptions of PSA Delivery

Video is a frequently used media for delivering drug prevention curriculum. Given the stress on identification, realism, and interest in curriculum development, it is important to assess the comparative perceptions of videos versus live performance. A Perception of Performance scale was developed and used to compare the two modalities for delivering drug prevention messages. The scale was developed using data from 334 undergraduate students at a large university in the southwestern United States. The age range was 17-42, median age of 19, 44% were female and 96% were European American. To validate the scale, 465 students in a single high school were randomly assigned to, either live or video performance conditions. 52% were female, 75% non-Hispanic White, 12% Hispanic, and 13% other. Participants viewed either a live performance or a video performance and then immediately completed the Perception of Performance Scale. Exploratory and Confirmatory Factor Analyses were conducted and three dimensions were identified: identification, interest, and realism with reliabilities of .86, .89, and .90 respectively. Live performance was perceived as significantly more interesting and realistic than video performance, suggesting that live performance may be a more effective medium for engaging high school aged youths. Miller, M., Hecht, M., and Stiff, J. An Exploratory Measurement of Engagement with Live and Film Media. *Journal of the Illinois Speech and Theatre Association*, 49, pp. 69-83, 1998.

The Lives, Motivations, and Options of Pregnant Drug Abusing Women, Their View

Extensive literature exists about the effects of drugs on the fetus but almost no information exists about the mother herself. Through interviews with 120 pregnant or recently delivered drug-using women, Dr. Sheigla Murphy and Dr. Marsha Rosenbaum examine how pregnant addicts make choices about their drug use, pregnancy, and prenatal care. To combat the stereotype of the negligent and even abusive pregnant drug user, the authors present the feelings and motivations of the women themselves. How do they decide whether to terminate their pregnancy? What options are available to them if they choose to continue the pregnancy but can't kick the drug use? Where do they get information upon which to make their decisions? They tend not to terminate pregnancy. They tend to change from one drug to another based on newspaper stories (if crack is bad, use heroin). The authors address these issues and the policy implications of their findings. Murphy, S. & Rosenbaum, M. Pregnant Women on Drugs: Combating Stereotypes and Stigma. New Brunswick, NJ: Rutgers University Press, 1999.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse
May, 1999**

Research Findings

Intramural Research

Molecular Neuropsychiatry Section, Cellular Neurobiology Branch

Methamphetamine-induced Increase of an Immediate Early Gene, *c-fos*, is Attenuated by Endogenous Opioid Peptide

Methamphetamine is a well-known psychostimulant of abuse that at high doses causes long-lasting neurotoxic effects. The mechanism underlying the neurotoxic action of methamphetamine is believed to involve free radical formation as well as the activation of certain immediate early genes. The immediate early genes are believed to be involved in the long-term effects of drugs of abuse by affecting the expression of other proteins that might be related to an altered state of physiology. In the past, the endogenous delta opioid peptide DADLE has been found by NIDA IRP scientists to prolong survival of peripheral organs such as the hearts and the lungs. NIDA IRP investigators also found that DADLE can block the dopaminergic terminal damage caused by methamphetamine and that DADLE can act as a free radical scavenger in vitro. More recent work has now found that DADLE blocks the increase of an immediate early gene *c-fos* in the area of brain that is most susceptible to the neurotoxic insult of methamphetamine. This constitutes the first report that a genomic influence exerted by a psychostimulant can be counteracted by an endogenous system. These data will be useful for understanding more about the physiological role of endogenous opioid peptides in the brain and pave an avenue for developing certain therapeutic approach for treating methamphetamine abuse. Hayashi, T., Tsao, L.-I., Cadet, J.L. and Su, T.-P. *European Journal of Pharmacology*, 366, pp. R7-R8, 1999.

Brain Imaging Section, Neuroimaging Branch

Age-dependent Dopamine Receptor Loss in Humans may be Overestimated

The relation between striatal dopamine D2 receptor binding and aging was investigated in rhesus monkeys with positron emission tomography (PET). Monkeys, ranging in age from 39 to 360 months, were scanned with ¹¹C-raclopride and binding potential in the striatum was estimated graphically. Because magnetic resonance imaging analysis revealed a concomitant relation between size of striatum and age, the dynamic PET data were corrected for possible partial volume artifacts. The age-related decline in binding potential was 1% per year and, importantly, was smaller than the apparent effect if the age-related change in size was ignored. The rate of decline in binding potential is consistent with in vitro findings in monkeys but smaller than what has been measured previously in humans using PET. Previous PET studies in humans, however, have not corrected for partial volume error, although a decline in striatal size with age has been demonstrated. The results of this study suggest that partial volume correction must be applied to PET data to accurately detect small changes in receptor binding that may occur in parallel with structural

changes in the brain in order not to overestimate the magnitude of the dopamine receptor loss. Morris, E.D., Chefer, S.I., Lane, M.A., Muzic Jr., R.F., Wong, D.F., Dannals, R.F., Matochik, J.A., Bonab, A.A., Villemagne, V.L., Grant, S.J., Ingram, D.K., Roth, G.S., and London, E.D. Loss of D2 Receptor Binding with Age in Rhesus Monkeys: Importance of Correction for Differences in Striatal Size. *J. Cereb. Blood Flow & Metab.*, 19(2), pp. 218-229, 1999.

Synthetic Route Developed for a Radiotracer Suitable for Imaging Nicotinic Acetylcholine Receptors in the Brain using SPECT

Interest in the normal and pathological roles of nicotinic acetylcholine receptors (nAChRs) within the brain has created a need for selective radiolabeled ligands that can be used to noninvasively image these receptors. This need has been addressed by devising simple radiochemical syntheses for 5-[125I]iodo-3-(2(S)-azetidylmethoxy)pyridine (5-[125I]iodo-A-85380) as well as 5-[123I]iodo-A-85380, by radioiodination of 5-trimethyltin-3-((1-tert-butoxycarbonyl-2(S)-azetidyl)methoxy)pyridine, followed by acidic deprotection. The average radiochemical yield was 50-65% and the average specific radioactivities of the I-125 and I-123 containing ligands were 2000 mCi/ μ mol and 7000 mCi/ μ mol, respectively. The binding affinity of both iodinated radioligands for nicotinic receptors was exceptionally high, 11.2 pM. Preliminary in vivo studies and ex vivo autoradiography in mouse brain demonstrated that 5-[125I]iodo-A-85380 selectively labels nicotinic receptor-rich regions with very high potency and specificity. These studies demonstrate the suitability of 5-[123I]iodo-A-85380 as a radioligand for single photon emission computed tomography (SPECT) imaging of nicotinic receptors within the brain. Horti, A.G., Koren, A.O., Lee, K.S., Mukhin, A.G., Vaupel, D.B., Kimes, A.S., Stratton, M., and London, E.D. Radiosynthesis and Preliminary Evaluation of 5-[123/125I]iodo-3-(2(S)-azetidylmethoxy)-pyridine: A Radioligand for Nicotinic Acetylcholine Receptors. *Nucl. Med & Biology*, 26, pp. 175-182, 1999.

Chemistry & Drug Metabolism Section, Clinical Pharmacology Branch

Intensity-Related Effects of Imagery Scripts on Tobacco Craving and Mood

Two experiments were conducted to determine whether active imagery would elicit tobacco craving in smokers with histories of drug abuse who were not interested in quitting smoking. In Experiment 1, we used scripts that contained positive, negative, or neutral affective content with and without descriptions of smoking urge. Scripts with urge content and negative affect scripts increased subjective reports of tobacco craving. An interaction between affective manipulation and urge content was observed on self-reported mood. In Experiment 2, positive affect scripts that varied in amount of urge content produced an orderly increase in tobacco craving as a function of urge intensity, suggesting that changes were specific to the imagery manipulation. In both experiments, increases in tobacco craving were positively correlated with craving for drug of choice, suggesting that stimuli that engender smoking urges may occasion craving for other drugs of abuse. Harris, N.A., Taylor, R.C., Singleton, E.G., and Heishman, S.J., *Poster, Society for Research on Nicotine and Tobacco, San Diego, California, 6 March 1999.*

Behavioral Pharmacology Section, Preclinical Pharmacology Laboratory

Chronic Caffeine Exposure Potentiates Nicotine Self-administration in Rats

The prevalence of tobacco smoking and coffee drinking place nicotine and caffeine among the most used licit drugs in many societies and their consumption is often characterized by concurrent use. The pharmacological basis for any putative interaction between these drugs remains unclear. Epidemiological reports support anecdotal evidence, which suggests that smokers consume caffeine to enhance the euphoric effects of nicotine. The scientists have recently examined the effects of chronic exposure to caffeine on self-administration responding maintained by nicotine in Sprague-Dawley rats. Rats consuming caffeine (approximately 150-180 mg/kg per day) in their drinking water for 7 days prior to the beginning and throughout behavioral testing acquired intravenous nicotine self-administration (0.03 mg/kg per infusion) more rapidly than did controls. In a cross-over design, exclusion of caffeine brought levels of nicotine self-administration back to baseline, while adding caffeine to the drinking water of control rats increased responding maintained by nicotine over 90%. These findings strongly suggest that caffeine can potentiate the reinforcing properties of nicotine, thus highlighting the importance of environmental factors in shaping and maintaining tobacco smoking. Shoab, M., Swanner, L.S., Yasar, S. and Goldberg, S.R. *Psychopharmacology*, 142, pp. 327-333, 1999.

Behavioral Effects of Nicotine, Amphetamine and Cocaine Under a Fixed-interval Schedule of Food

Reinforcement in Rats Chronically Exposed to Caffeine

Epidemiological surveys demonstrate that caffeine, the main psychoactive ingredient of coffee, is a positive correlate in drug abuse. To characterize the behavioral nature of caffeine interactions with other psychomotor stimulants, IRP scientists examined the effects of chronic caffeine exposure on the behavioral responses to nicotine, amphetamine, cocaine, the selective D1 agonist SKF-82958 and the selective D2 receptor agonist NPA, in rats responding under a fixed interval (FI) schedule of food reinforcement. Following stabilization of responding, Sprague-Dawley rats were divided into two groups; one maintained on tap water (control) and the other on caffeine (3 mg/ml added to the drinking water). Rats developed complete tolerance to the effects of caffeine in the drinking water over 5 days of caffeine exposure. After behavior stabilized, effects of drugs were evaluated. Nicotine, amphetamine and cocaine each produced biphasic dose-dependent changes in response rate with maximum increases in response rate following immediate doses and decreases in response rates following higher doses. The increase in rates of responding produced by amphetamine or cocaine (but not nicotine) were greater in caffeine-drinking than in water-drinking rats. Both SKF-82958 and NPA produced only dose-dependent decreases in rates of responding. Caffeine-drinking rats were less sensitive to the rate-depressant effects of SKF-82958 than water-drinking rats. However, similar changes were produced by NPA in both groups. Chronic exposure to caffeine produced complete insurmountable tolerance to the response-rate increasing (stimulant) effects of acute caffeine in caffeine-drinking rats. In conclusion, this study revealed that chronic caffeine exposure potentiates the behavioral response to amphetamine and cocaine but not to that of nicotine in rats responding under a FI schedule of food reinforcement. Thus, it is likely that these effects are mediated through different pharmacological mechanisms. Jaszyna, M., Gasior, M., Shoaib, M., Yasar S. and Goldberg, S.R. *Psychopharmacology*, 140, pp. 257-271, 1998.

Alteration of the Discriminative Stimulus Effects of Nicotine in Rats by Chronic Exposure to Caffeine

Caffeine and nicotine are the main psychoactive ingredients of coffee and tobacco, with a high frequency of concurrent use in humans. IRP scientists examined the effects of chronic caffeine exposure on the acquisition and the pharmacological characteristics of a nicotine discrimination in Sprague-Dawley rats. Once rats learned to lever-press reliably under a fixed-ratio schedule for food pellets, they were divided into two groups; 12 animals were maintained continuously on caffeine (3 mg/ml) added to the drinking water and another 12 control rats continued to drink tap water. Both water- and caffeine-drinking groups required a comparable number of training sessions to attain reliable stimulus control. The nicotinic-receptor antagonist mecamylamine blocked the discriminative effects of nicotine with comparable potency and efficacy in water- and caffeine-drinking groups. There was a dose-related generalization to nicotine cue in water-drinking rats after i.p. treatment with d-amphetamine, cocaine, the selective dopamine uptake inhibitor GBR-12909, apomorphine, and the selective dopamine D1 receptor agonist SKF-82958, but not in caffeine-drinking rats. There was no generalization to the nicotine cue after i.p. treatment with caffeine or the selective D2 (NPA) and D3 (PD 128,907) dopamine-receptor agonists in either water- or caffeine-drinking rats. The dopamine-release inhibitor CGS 10746B reduced the discriminative effects of nicotine in water-drinking rats, but not in caffeine-drinking rats. Thus, chronic caffeine exposure (average, 135 mg/kg/day) did not affect the rate of acquisition of the nicotine discrimination, but it did reduce the dopaminergic component of the nicotine-discriminative cue. The reduction was permanent, as this effect was still evident after the caffeine solution was replaced with water in caffeine-drinking rats. That nicotine could reliably serve as a discriminative stimulus in the absence of the dopaminergic component of its discriminative cue may differentiate nicotine from "classical dopaminergic" drugs of abuse such as cocaine and amphetamine. Gasior, M., Shoaib, M., Yasar, S., Jaszyna, M. and Goldberg, S.R. *Journal of Pharmacology and Experimental Therapeutics*, 288, pp. 1053-1073, 1999.

Effects of Dopamine- and Serotonin-releasing Agents on Methamphetamine Discrimination and Self-administration

Although most behavioral effects of methamphetamine are mediated by the dopaminergic neurotransmitter system, neurochemical findings suggest that there also is strong involvement of serotonergic neurotransmission. To analyze the relative involvement of dopamine and serotonin in the behavioral properties of methamphetamine, IRP scientists tested two amphetamine analogs that selectively release either brain dopamine (phentermine) or serotonin (fenfluramine) in Sprague Dawley rats. These compounds were tested for their ability to substitute for methamphetamine in rats trained to discriminate methamphetamine from saline and, subsequently, for their ability to alter methamphetamine self-administration. The dopamine releaser phentermine decreased methamphetamine self-administration, but only at a dose that fully generalized to the methamphetamine stimulus in the discrimination study. The serotonin releaser fenfluramine attenuated methamphetamine self-administration to a much larger extent than phentermine and did so at doses that did not generalize to methamphetamine and did not decrease rate of responding for food. These results suggest that dopamine release plays a dominant role in the subjective effects of methamphetamine. However, stimulation of serotonin release can strongly modify methamphetamine self-administration. Munzar, P., Baumann, M.H., Shoaib, M. and Goldberg, S.R. *Psychopharmacology*, 141, pp. 287-296, 1999.

Potiation of the Discriminative-stimulus Effects of Methamphetamine by a Histamine h4 Receptor Antagonist

Most behavioral effects of methamphetamine appear to be related to the release of dopamine. Recent findings, however, suggest that histamine release may also contribute to its actions. Endogenous histamine release is regulated by histamine h4 autoreceptors. Their blockade by the h4 antagonist thioperamide may increase histamine release, thus augmenting methamphetamine's behavioral effects. To test this hypothesis, IRP researchers tested thioperamide in rats discriminating methamphetamine from saline. Thioperamide potentiated the discriminative-stimulus effects of methamphetamine and this effect was reversed by co-administration of R-alpha-methylhistamine, a h4 agonist. These data suggest that methamphetamine's behavioral effects are modified by drugs affecting histamine release. This knowledge may result in the development of new strategies for the treatment of psychostimulant abuse. Munzar, P., Nosal, R. and Goldberg, S.R. *European Journal of Pharmacology*, 363, pp. 93-101, 1998. Discrimination and Self-administration of Nicotine by Inbred Strains of Mice The discriminative stimulus effects of nicotine have been characterized by IRP scientists in two inbred strains of mice that differ in many pharmacological responses. They have also investigated the feasibility of intravenous self-administration studies with nicotine in one of the strains. For discriminative studies, three groups of C57BL/6 and one group of DBA/2 mice were trained in a two-lever operant conditioning paradigm with a tandem schedule of food reinforcement. After 40 sessions, accuracy reached 57.5, 77.5 and 90.0% in C57BL/6 mice trained with (-)-nicotine (SC) in doses of 0.4, 0.8 and 1.6 mg/kg, respectively. DBA/2 mice trained with 0.8 mg/kg nicotine attained similar (73.3%) accuracy. All groups of mice yielded orderly dose-response curves for nicotine. Rates of responding in the undrugged state were lower for DBA/2 than for C57BL/6 mice; DBA/2 mice were also slightly less sensitive than C57BL/6 mice to the response rate-reducing effect of nicotine. The nicotine antagonist mecamlamine blocked the discriminative stimulus effect of nicotine in all groups. In the intravenous self-administration study, nicotine served as a positive reinforcer in drug-naive C57BL/6J mice. The methods described provide possible approaches for genetic analyses of strain differences in sensitivity to the discriminative and reinforcing stimulus properties of nicotine. Stolerman, I.P., Naylor, C., Elmer, G.I. and Goldberg, S.R. *Psychopharmacology*, 141, pp. 297-306, 1999.

Clinical Trials Section, Treatment Branch

Occurrence of Cocaine in Urine of Substance Abuse Treatment Patients

As part of ongoing research efforts to improve methods of monitoring drug use in treatment patients, the presence of cocaine in urine specimens was evaluated as a possible marker for recent illicit cocaine use. A total of 2,327 urine specimens collected during a clinical trial of a cocaine abuse treatment study were tested. Cocaine was measured by gas chromatography-mass spectrometry and benzoylecgonine equivalents were determined by fluorescence polarization immunoassay (FPIA). More than one-third of the specimens were positive (>25 ng/mL) for cocaine, and nearly two-thirds were positive (> 300 ng/mL) for cocaine metabolite. Median concentrations of cocaine and benzoylecgonine equivalents were 235 and 14,900 ng/mL and maximum concentrations were 112,025 and 1,101,190 ng/mL in cocaine- or benzoylecgonine-positive specimens, respectively. No significant differences in cocaine or benzoylecgonine concentrations between White and African American or between male and female patients were found. Cocaine was present less frequently and at lower concentrations than benzoylecgonine, but more frequently than expected based on an approximate average half-life of 1 hour. These results suggest that cocaine may exhibit a longer terminal half-life and/or that accumulation of cocaine can occur in chronic, heavy users. Preston, K.L., Goldberger, B.A., and Cone, E.J. Occurrence of Cocaine in Urine of Substance Abuse Treatment Patients. *Journal of Analytical Toxicology*, 22, pp. 580-586, 1998.

The Influence of an Instruction on the Stimulus Effects of Drugs in Humans

Volunteers (N = 14) participated in two experiments differing only in instructional set using a standard drug discrimination paradigm. In each experiment subjects were trained to discriminate between 75 mg tripeleminamine and placebo in 15 training sessions. In one experiment (SED), participants were instructed that one of the two drugs was more sedative-like than the other drug and during the other experiment (STIM), one of the two drugs was more stimulant-like. The experiments were otherwise the same. Order of presentation of the experiments was counterbalanced across participants. During generalization tests, participants received capsules that contained diazepam (2.5 and 5 mg) or d-amphetamine (5 and 10 mg). Tripeleminamine and placebo were discriminated on approximately 65% of sessions with no differences across experiments. Tripeleminamine increased in scores on subjective effects scales measuring sedative effects and decreased in scores on scales measuring stimulant effects across both experiments. Amphetamine and diazepam each produced typical changes in stimulant and sedative effects, respectively, with only minor differences between experiments. Some subjective effects of the training and

test drugs differed between experiments with more sedative and less stimulant and anxiety effects during SED relative to during STIM. In SED and STIM, capsules were labeled over 80% of the time as a sedative and stimulant, respectively. These results indicate that instructions designed to give participants expectations as to the types of drugs they would be administered produced no effect on discrimination and only a few significant changes in subjective effects. On the other hand, when participants were asked to name (label) the drug they believed they received, their answers reflected the instructional set. Johanson, C.-E., and Preston, K.L. The Influence of an Instruction on the Stimulus Effects of Drugs in Humans. *Experimental and Clinical Psychopharmacology*, 6, pp. 427-432, 1998.

Improvement in Naltrexone Treatment Compliance with Contingency Management

Clinical experience has shown that poor compliance with naltrexone treatment seriously compromises its clinical utility. This study tested the efficacy of a voucher-based incentive program for improving compliance with naltrexone treatment. Opioid-dependent patients who had recently completed opioid withdrawal treatment were enrolled in a 12-week outpatient treatment research program in which they received naltrexone three times weekly and counseling once weekly. Subjects were randomized to three treatment groups: 1) Contingent (N = 19) - vouchers earned for each ingested naltrexone dose; 2) Non-Contingent (N = 19) - vouchers given at rates and values matched to the Contingent Group but independent of naltrexone ingestion; and 3) No Vouchers (N = 20) - no vouchers were available. The vouchers had monetary value and were exchangeable for goods and services. The Contingent group had significantly longer treatment retention and ingested significantly more doses of naltrexone (consecutive and total) than either control group. Voucher incentives can significantly increase adherence to naltrexone maintenance in recently detoxified opioid dependent individuals. Preston, K.L., Silverman, K., Umbricht, A., DeJesus, A., Montoya, I.D., and Schuster, C.R. Improvement in Naltrexone Treatment Compliance with Contingency Management. *Drug and Alcohol Dependence*, 54, pp. 127-135, 1999.

Cellular Neurophysiology Section, Cellular Neurobiology Branch

Phenotypic Characterization of GFR alpha-1 Expressing Neurons

The glial cell line-derived neurotrophic factor (GDNF) rescues motoneurons and nigral dopaminergic (DA) cells from induced cell death in different species of animals. In addition, GDNF results in a remarkable improvement of behavioral functions in Parkinsonian monkeys. A high affinity receptor for GDNF has been cloned (GFR alpha-1), whose pattern of expression indicates that it is not restricted to those brain areas containing motoneurons and DAergic cells. These observations suggest that GDNF may activate a number of different sub-types of brain cells. IRP scientists have found that GFR alpha-1 is expressed in defined populations of neurons. As anticipated, GFR alpha-1 occurs in DAergic cells of the substantia nigra compacta (SNC) and the ventral tegmental area (VTA). GFR alpha-1 is also present in GABAergic cells located either in the lateral SNC or in the substantia nigra reticulata (SNR), and these GABAergic cells are more abundant in the caudal levels of the SNR. Results imply that GDNF-induced improvements in the behavior of semi-parkinsonian animal models may, in part, involve GABAergic cells of the SNR. Using either a cerebral ischemia model (middle cerebral artery, MCA ligation) or physical cortical injury, IRP investigators found a robust up-regulation of GFR alpha-1 expression in granule cells ipsilateral to the area receiving the insult. In both models, GFR alpha-1 up-regulation peaks 6 hours following ischemia or physical injury. These results indicate that GFR alpha-1 might be part of an endogenous neuroprotective system that is activated following brain insult or injury and may act as a defense mechanism in the brain. Okada, Y. et al. Experimental Implication of Celiac Ganglionotropic Invasion of Pancreatic-Cancer Cells Bearing C-Ret Proto-Oncogene with Reference to Glial-Cell-Line-Derived Neurotrophic Factor (GDNF). *Int J Cancer*, 81(1), pp. 67-73, Mar 31, 1999. Perez-Navarro, E. et al. Intrastratial Grafting of a GDNF-Producing Cell Line Protects Striatonigral Neurons from Quinolinic Acid Excitotoxicity In Vivo. *Eur J Neurosci*. 11(1), pp. 241-249, Jan 1999. Enokido, Y. et al. GFR Alpha-4 and the Tyrosine Kinase Ret Form a Functional Receptor Complex for Persephin. *Curr Biol*. 8(18), pp. 1019-1022, Sep 10, 1998. Trupp, M. et al. Multiple GPI-Anchored Receptors Control GDNF-Dependent and Independent Activation of the C-Ret Receptor Tyrosine Kinase. *Mol Cell Neurosci*. 11(1-2), pp. 47-63, May 1998. Hishiki, T. et al. Glial Cell Line-Derived Neurotrophic Factor/Neurturin-Induced Differentiation and its Enhancement by Retinoic Acid in Primary Human Neuroblastomas Expressing C-Ret, GFR Alpha-1, and GFR Alpha-2. *Cancer Res*. 58(10), pp. 2158-2165, May 15, 1998.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****May, 1999**

Program Activities

Program Announcements/RFAs

On April 29, 1999, NIDA issued a Program Announcement entitled **Clinical Research Education Programs in Drug Abuse and Addiction** (PAR-99-093). This PA invites grant applications to support educational programs aimed at 1) developing the research skills of investigators who wish to focus on clinical, prevention, health services, or treatment issues in drug abuse or 2) developing a cadre of clinical drug abuse experts proficient in the use of research findings to develop or implement early detection, diagnosis, treatment or prevention interventions.

On March 31, 1999, numerous NIH components (including NIDA) and the CDC issued a Program Announcement entitled **Research on Ethical Issues in Human Studies** (PA-99-079) to solicit grant applications for support to conduct research on ethical issues that arise with research involving human participants.

On April 13, 1999, numerous NIH Institutes (including NIDA) issued a Program Announcement entitled **Mentored Quantitative Research Career Development Award** (PA-99-087) which is intended to support the career development of investigators with quantitative scientific and engineering backgrounds outside of biology or medicine who have made a commitment to focus their research endeavors on behavioral and biomedical research (basic or clinical).

On April 20, 1999, NIDA, in conjunction with the National Institute of Mental Health, the National Institute on Alcohol Abuse and Alcoholism, and the National Institute of Environmental Health Sciences issued a Program Announcement entitled **Individual Predoctoral National Research Service Awards for M.D./Ph.D. Fellowships** (PA-99-089). The purpose of the fellowship program described in this announcement is to help ensure that highly trained physician/scientists will be available in adequate numbers and in the appropriate research areas and fields to meet the Nation's mental health, drug abuse and addiction, alcohol abuse and alcoholism, and environmental health sciences research needs.

On March 5, 1999, numerous NIH components (including NIDA) issued an RFA entitled **Technologies for Generation of Full-Length Mammalian cDNA** (CA-99-005). The purpose of this RFA is to support the development of technologies that will facilitate the generation of a complete set of full-length human cDNAs as well as other mammalian cDNAs. Letter of Intent Receipt date for this RFA was April 6, 1999, and the Application Receipt date was May 13, 1999.

On March 5, 1999, numerous NIH Institutes (including NIDA) issued an RFA entitled **Rat Genome Database** (HL-99-013). The objective of this RFA is to establish a database that will collect, consolidate, and integrate data generated from ongoing rat genetic, genomic, and related research efforts, and to make these data widely available to the

scientific community. Letter of Intent Receipt date for this RFA was April 1, 1999, and the Application Receipt date was April 26, 1999.

On March 8, 1999, numerous NIH components (including NIDA) issued an RFA entitled **Centers for Dietary Supplements Research: Botanicals** (OD-99-007). The major goal of this RFA is to foster multidisciplinary research in order to develop systematic evaluation of the safety and efficacy of botanicals. Letter of Intent Receipt date for this RFA was April 13, 1999, and the Application Receipt date was May 13, 1999.

On March 16, 1999, NIDA, in conjunction with the NIH Child Abuse and Neglect Workgroup, issued an RFA entitled **Research on Child Neglect** (OD-99-0006). This RFA solicits investigator-initiated applications for research on child neglect (contrasted to abuse) including but not limited to antecedents and consequences of neglect--socio-emotional and developmental neurobiology (mechanisms of stress system activation on brain anatomic and functional development, ages of vulnerability to neglect on brain development)--the processes and mediators of risk and protective factors, treatment, preventive interventions, and service delivery. Letter of Intent Receipt date for this RFA is June 15, 1999, and the Application Receipt date is September 14, 1999.

On March 31, 1999, NIDA, in conjunction with several other NIH Institutes, issued an RFA entitled **Mouse Mutagenesis and Phenotyping: Nervous System and Behavior** (MH-99-007). The purpose of this RFA is to establish facilities for large-scale mutagenesis and phenotyping of nervous system functions and complex behaviors in the laboratory mouse. Neuroscience-focused mutagenesis and phenotyping facilities established by this RFA are expected to serve as a national resource by producing a bank of mouse strains that harbor a wide range of mutations affecting murine nervous system function and behavior. Data and biomaterials produced in projects supported under this RFA will be made widely available to the scientific community. Receipt date for this RFA is August 2, 1999, and the Application Receipt date is October 14, 1999.

Other Program Activities

Training Program in Medications Development for Drugs of Abuse

The Medications Development Division will award its first training grant ("Training Program in Medications Development for Drugs of Abuse, T32 DA07312, PS 140), beginning July 1, 1999, to Dr. Alexandros Makriyannis, a professor of Medicinal Chemistry and Molecular and Cell Biology at the University of Connecticut. The program is designed to train four predoctoral and four postdoctoral trainees in the first year, with additional students and postdoctoral fellows being added to the program in subsequent years. The training will offer traditional medicinal chemistry, combined with high throughput and combinatorial approaches currently utilized in the pharmaceutical industry, as well as the pharmacological and clinical aspects of drug development. The State of Connecticut recently built the Center for Drug Discovery at the University of Connecticut in support of the University's longstanding academic commitment to drug and alcohol abuse research. The collaborations which the Center has with Brookhaven National Laboratory, the Torrey Pines Institute, Bristol-Myers Squibb, Pfizer, and other companies within the private sector who will make their laboratories available for training purposes, will provide a unique training opportunity for the students and postdoctoral fellows being trained under this grant.

NIDA/Somerset Pharmaceuticals CRADA

NIDA and Somerset Pharmaceuticals have executed a Letter of Intent for a Cooperative Research and Development Agreement to conduct clinical testing of selegilene in both immediate release and transdermal patch formulations, as a potential pharmacotherapy for the treatment of cocaine dependence.

Buprenorphine Office-Based Study

The Medications Development Division is conducting a Buprenorphine Office-Based Study. This is an open label study that will be conducted in six states (San Antonio, Texas; New York, New York; Chicago, Illinois; Tampa, Florida; Los Angeles, California; and Seattle, Washington). A total of six hundred patients will be enrolled. Investigator meetings

have been held in Seattle and New York. An investigator meeting is slated for mid-May in Los Angeles. The trial is scheduled to start enrolling patients in the 2nd Quarter of 1999. The study will evaluate opiate abuse treatment using buprenorphine/naloxone in settings other than the traditional narcotic treatment programs. Information will be obtained to: 1) assess the safety of expanding buprenorphine/naloxone treatment to an adolescent population; 2) develop and test materials, for physicians, that will be useful in training courses by professional societies, and 3) allow labeling changes for induction, maintenance and detoxification regimens using buprenorphine/naloxone in 600 patients.

Amantadine and Disulfiram Reviews

The Medications Development Division held a consultant review of two medications and clinical data (Amantadine and Disulfiram) on April 26 preparatory to future clinical development plans. Data on these two compounds was developed by NIDA P-50 Medications Development Center grantees.

Lofexidine Meeting

On April 7, MDD and Britannia Pharmaceuticals/Forum Products participated in an end of Phase II meeting with the FDA regarding lofexidine, an alpha adrenergic agonist for the treatment of opiate withdrawal. Comments were received regarding the lofexidine development plan.

NIDA/IRP Summer Research Program for Students

Since 1986, the IRP has had a summer research program for students. During the summer of 1998, a total of 41 students representing 35 high schools, colleges, and medical and graduate schools participated in the program through either the NIH Summer Internship Program or the Minority Research and Training Program. Each student participant was assigned to work with an IRP scientist on a research project. The students' training program is individually developed and includes directed readings, tutorials, attendance at seminars, and actual laboratory experience under the direction of the scientist. The culmination of the summer program is the students' presentation of their research at the NIH Student Poster Session held at the Bethesda campus in early August. Because of outstanding contributions and effort, some students will be co-authors on published papers or abstracts. The NIH Summer Internship Program is coordinated by Dr. Stephen Heishman, and the Minority Research and Training Program is coordinated by Dr. Jean Cadet and Ms. Mary Affeldt.

NIDA's New and Competing Continuation Awards Since February 1999

Avants, Sandra A. --- Apt Foundation

Reducing HIV Risk in Methadone-Maintained Patients

Bannon, Michael J. ---Wayne State University School of Medicine

Cocaine Binding Dopamine Transporter: Molecular Biology

Bellack, Alan S. ---University of Maryland

The Process of Change in Drug Abuse by Schizophrenics

Berridge, Craig W. --- University of Wisconsin

Neurochemistry of Amphetamine Induced Arousal

Bickel, Warren K. --- University of Vermont

Impulsivity in Drug Dependence: Delay Discounting

Bidlack, Jean M. --- University of Rochester

Partial Opioids: Potential Treatments for Cocaine Abuse

Biglan, Anthony --- Oregon Research Institute

Low-Cost Prevention of Conduct Disorders

Booth, Robert E. --- University of Colorado
HIV Risk in Drug Users: Relapse and Maintenance Behavior

Brook, David --- Mount Sinai School of Medicine
AIDS Risk: Puerto Rican IDU Fathers and Their Children

Cadoret, Remi J. --- University of Iowa-College of Medicine
Gene-Environment Interaction in Etiology of Drug Abuse

Caine, Barak S. --- Mclean Hospital
Cocaine Self-Administration in Dopamine 'Knockout' Mice

Calloway, Michael --- University of North Carolina at Chapel Hill
Predictors of SA - MH Program Linkages

Carroll, Frank I. --- Research Triangle Institute
Development of Ligands for Nicotinic Receptors

Chavkin, Charles --- University of Washington
Models of Opioid Receptor Desensitization Mechanisms

Chow, Sherry H. --- University of Arizona
Direct Nose-Brain Drug/Peptide Transport

Cicero, Theodore J. --- Washington University
Opiate-Endocrine Interactions-Developmental Aspects

Cochrane, Carolyn E. --- Medical University of South Carolina
Career/Training in Drug Abuse Research

Comer, Sandra D. --- Research Foundation Mental Hygiene, Inc.
Buprenorphine Abuse by Humans: Laboratory Studies

Compton, Wilson M. --- Washington University
Over-the-Counter Syringe Purchase in Five Communities

Connors, Barry W. --- Brown University
Nicotinic Mechanisms in Sensory Neocortex

Cook, Royer F. --- ISA Associates Inc.
A Workplace CD-ROM Drug Prevention Program for Parents

Derrick, Brian E. --- University of Texas
Associative LTP of Area CA3 in the Hippocampus In Vivo

Deutsch, Howard M. --- Georgia Institute of Technology
Preclinical Development of Drugs for Stimulant Abuse

Duncan, Gary --- University of North Carolina-Office of Grants and Contracts
Elementary School Neuroscience Literacy

El-Bassel, Nabila --- Columbia University
HIV Risk and Partner Violence: Men on Methadone

Ellickson, Phyllis I. --- Rand Corporation
HIV Risk, Drugs, and Violence

Elliot, Diane I. --- Oregon Health sciences University
School-Based Drug Use Prevention for Girl Athletes

Epstein, Jennifer A. --- Cornell University-/Weill Medical College
Predictors of Adolescent Drug Use among Inner-city Youth

Evins, Eden A. --- Massachusetts General Hospital
Smoking Cessation in Schizophrenia

Fields, Howard I. --- University of California
Neural Substrate of Opiate Analgesia

Fisher, Philip A. --- Oregon Social Learning Center
Indian Wellness Preventive Intervention Project

France, Charles P. --- Louisiana State University Medical Center
Behavioral Pharmacology of Opioids

France, Charles P. --- Louisiana State University School of Dentistry
Discriminative Effects of Benzodiazepine Withdrawal

Freeborn, Donald K. --- Kaiser Foundation Hospitals
Drug Abuse Treatment Costs of Medicaid Clients in an HMO

Frost, James J. --- Johns Hopkins University
Brain Opioid Receptors and Cognition in Cocaine Abuse

Galanter, Marc --- New York University School of Medicine
Network Therapy Development, Stage II with Buprenorphine

Gallagher, Joel P. --- University of Texas Medical Branch
CRF Mechanisms and Cocaine

Gariti, Peter --- University of Pennsylvania
Combining a Smoke Ending Aid with Behavioral Treatment

Geyer, Mark A. --- University of California-San Diego
Monoamine and Hallucinogen Effects on Rodent Behavior

Ghasemzadeh, Mohammadhossein B. --- Washington State University
R03: Glutamate Receptor and Chronic Cocaine

Glassco, William S. --- Virginia Commonwealth University
Synthetic Exploration of Central Nicotinic Receptors

Glennon, Richard A. --- Virginia Commonwealth University
Chemical/Behavioral Studies on Hallucinogenic Agents

Goeders, Nicholas E. --- Louisiana State University Medical Center School of Medicine
Environmental Influences on Cocaine Self-Administration

Gollub, Randy I. --- Massachusetts General Hospital East
FMRI of Cocaine Effects in Cocaine Abusing Schizophrenic

Griffiths, Roland R. --- Johns Hopkins Bayview Medical Center
Benzodiazepines Use/Abuse: Effects on Memory Mechanisms

Hagan, Holly C. --- Seattle-King County Public Health Department
Hepatitis C in IDUs: Epidemiology and Prevention

Hammond, Donna I. --- University of Chicago
Effect of Inflammatory Nociception on Medullary Neurons

Harris, Debra S. --- University of California
Effects of Cortisol on Human Methamphetamine Response

Hogue, Aaron T. --- Fordham University
Family Change Mechanisms in Adolescent Drug Use Therapy

Hughes, John R. --- University of Vermont and State Agricultural College
Evaluation of a Cigarette Substitute

Inciardi, James A. --- University of Delaware
HIV/AIDS Risk Reduction among Drug-Involved Probationers

Inturrisi, Charles E. --- Cornell University Medical College
Glutamatergic Systems in Pain and Opioid Action

Jevtovic-Todorovic, Vesna --- Washington University
Psychotic and Analgesic Actions of NMDA Antagonists

Johnson, Bankole A. --- University of Texas Health Science Center
Cocaine Brain Effects and Neuroimaging

Johnson, Kenneth M. --- University of Texas Medical Branch
Neurochemical Pharmacology of Phencyclidine

Kalyuzhny, Alexander E. --- University of Minnesota
Opioid-GABA Interactions and Antinociception

Kaplan, Howard B. --- Texas A&M University
Drug Abuse and Other Deviant Adaptations to Stress

Kelley, Ann E. --- Wisconsin Psychiatric Institute and Clinic
Opioid Systems in Ventral Striatum and Food Reward

Kharasch, Evan D. --- University of Washington
Opioids in Cancer Pain and Drug Abuse: Optimizing Therapy

Kidorf, Michael S. --- Johns Hopkins Bayview Medical Center
Community-Based Intervention at Needle Exchange Sites

Kinnunen, Taru --- Harvard School of Dental Medicine
Exercise and Nicotine Replacement for Female Smokers

Knuepfer, Mark M. --- Saint Louis University
Cardiovascular Effects of Cocaine

Kolesnikov, Yuri A. --- Sloan-Kettering Institute-Cancer Research
Opioid and Non-Opioid Mechanism(s) of Neuropathic Pain

Koob, George F. --- Scripps Research Institute
Neuronal Substrates of Cocaine Reward

Kuhar, Michael J. --- Emory University
Mechanisms of Drugs of Abuse

Kuhn, Donald M. --- Wayne State University
The Neurotoxicity of Amphetamines and Related Stimulants

Langenbucher, James W. --- Rutgers State University of New Jersey
Neuroadaptive Clinical Models of Drug Dependents

Lennox, Richard D. --- Piedmont Research Institute, Inc.
The Impact of State Continuum-of-Care Mandates

Levine, Allen S. ---VA Medical Center
The Effect of Sucrose and/or Fat Ingestion on Opioids

Levin, Edward D. --- Duke University
Attention as a Target of Intoxication

Lindberg, Iris --- Louisiana State University Medical Center
Opioid Peptide Synthesizing Enzymes

Liu-Chen, Lee-Yuan --- Temple University School of Medicine
Regulation of Kappa Opioid Receptors

Lluedtke, Robert R. --- University of North Texas Health Science Center
Therapeutics for Cocaine Dependence: Natural Products

Lukas, Scott E. --- Alcohol and Drug Abuse Research Center
Medication Development for Cocaine Abuse: CDP-Choline

Mackler, Scott A. --- VA Medical Center
Nac-1, a Cocaine-Regulated MRNA in the Rat Brain

Makriyannis, Alexandros --- University of Connecticut
Dopamine Transporter Ligands as Cocaine Medications

Malison, Robert T. --- Yale University School of Medicine
Advanced Training in Spectrum/PET Neuroreceptor Imaging

Margolin, Arthur --- Substance Abuse Treatment Center
Optimizing Auricular Acupuncture for HIV+ Drug Abusers

Marks, Michael J. --- University of Colorado
Alpha-Conotoxin MII: A Selective Nicotinic Receptor Problem

Marshall, John F. --- University of California-Irvine
Methamphetamine Abuse and Cortical Cell Injury

Martin, Billy R. --- Temple University School of Medicine
College on Problems of Drug Dependence Meeting

Masson, Carmen I. --- University of California-San Francisco
Prevention of Infectious Disease in Injection Drug Users

McCance-Katz, Elinore --- Montefiore Medical Center
Opioids and HIV Medications-interactions in Drug Abusers

Mendelson, John --- University of California
Clinical Pharmacology of Methamphetamine Stereoisomers

Meyer, Jerrold S. --- University of Illinois-@uc-Department of Veterinary Biosciences
Receptors for Abused Drugs: Development and Plasticity

Morgenstern, Hal --- University of California-Los Angeles
Marijuana Use and the Risks of Lung and Other Cancers

Morrow, Kathleen M. --- Brown University
Reducing HIV Risk in Substance Abusing Women: A Pilot

Murphy, Sheigla --- Institute for Scientific Analysis
An Ethnography of Victimization, Pregnancy and Drug Use

Musto, David F. --- Yale University
American Women and Substance Abuse 1865-1980

Najavits, Lisa M. --- Mclean Hospital
The Efficacy of Psychosocial Therapies for Drug Abuse

Napier, Celeste T. --- Loyola University Chicago
Opioids and the Physiology of the Ventral Pallidum

Neaigus, Alan --- National Development and Research Institute
Non-Injecting Heroin Users, New Injectors and HIV Risk

Nemoto, Tooru --- University of California-San Francisco
HIV-Related Behaviors in Hard to Reach High Risk Men

Nestler, Eric J. --- Yale University School of Medicine
Molecular Studies of Opiate and Cocaine Action in Brain

Olsen, George D. --- Oregon Health Sciences University
Morphine-6 Glucuronide: Development of Breathing Control

Page, John B. --- University of Miami School of Medicine
Drug Use and Gang Activity among Haitian Youths

Perlman, David C. --- Beth Israel Medical Center
TB Screening and Prevention in Active Users

Porreca, Frank --- Arizona Health Sciences Center
Bifunctional Opioid/CCK Ligands for Pain

Proudfit, Herbert K. --- University of Illinois
Pharmacologic Studies of CNS Pain Modulatory Systems

Raso, Victor A. --- Boston Biomedical Research Institute
Vaccine to Elicit Catalytic Anti-Cocaine Antibodies

Rayport, Stephen G. --- Columbia University
Psychostimulant Sensitization at the Synaptic Level

Rebec, George V. --- Indiana University
Neuropharmacology of Drugs of Abuse: Amphetamine

Renshaw, Perry F. --- Mclean Hospital
Magnetic Resonance, EEG and Behavior after Cocaine

Ricaurte, George A. --- Johns Hopkins University
Studies of Substituted Amphetamine Neurotoxicity

Richter, Anke --- Research Triangle Institute
Extended Economic Impact Assessment of AIDS Intervention

Rosenberg, Gary --- Mount Sinai School of Medicine
Drug Use: Generational Transmission in Minority Youth

Rose, Jed E. --- Duke University Medical Center
Scaling the Reinforcing Value of Cigarette Smoke

Roy, Sabita --- VA Medical Center
Role of Mu-Opioid Receptor in Immune Function

Rubenstein, John I. --- University of California
NKX Homeobox Gene Regulation of Ventral CNS Development

Sadee, Wolfgang --- University of California-San Francisco
Opioid Receptor Regulation

Schenk, James O. --- Washington State University
Drugs of Abuse and Dopamine Release and Reuptake

Sharp, Burt M. --- University of Tennessee
Interaction between Nicotine and Stress

Siggins, George R. --- Scripps Research Institutes
Morphine-like Brain Peptides--Cellular Neurobiology

Simon, Eric J. ---New York University Medical Center
Biochemical Research on Opioid Receptors

Simon, Eric J. ---New York University Medical Center
30th Annual International Narcotics Research Conference

Singer, Merrill --- Hispanic Health Council
Syringe Access and HIV Risk

Smith, James E. --- Bowman Gray School of Medicine
Center for Neurobiological Investigation of Drug Abuse

Sorg, Barbara A. --- Washington State University
Cortical Regulation of Sensitization

Spealman, Roger D. --- Harvard Medical School
Behavior Controlled by Drug Injections

Szapoznik, Jose --- University of Miami
Structural Ecosystems Treatment with Drug using Minority Youth

Tashkin, Donald P. --- UCLA Department of Medicine
Pathophysiologic Consequences of Smoked Substance Abuse

Thayer, Stanley A. --- University of Minnesota
HIV Neurotoxicity: Mechanism and Modulation Y Canabinoids

Vezenia, Paul --- University of Chicago
Glutamate and the Self Administration of Amphetamines

Waldron, Holly B. --- University of New Mexico
Resistant Adolescent Substance Abusers in Treatment

Weber, Richard J. --- University of Illinois
Neuroendocrine-Immune Correlates of Self-Administered Heroin

Wilcox, George I. --- University of Minnesota
Spinal Mechanisms of Opioid Tolerance

Wilens, Timothy E. --- Massachusetts General Hospital
Long-Term Drug Abuse in ADHD

Williams, Mark I. --- Nova Research Company
Condom Use Among Drug Users Receiving Antiretrovirals

Wilson, Marlene A. --- University of South Carolina
Gender Differences in the Brain and Behavior

Wilson, William H. --- Duke University Medical Center
Early Use of Marijuana and Brain Morphology and Function

Winkleby, Marilyn A. --- Stanford University School of Medicine
High Risk Teen Tobacco Use Prevention through Advocacy

Yurgelun-Todd, Deborah A. --- Mclean Hospital
Residual Cognitive Effects of Cannabis: An FMRI Study

Yu, Xiao-Fang --- Johns Hopkins University School of Public Health
Viral Determinants of Disease Progression in HIV+ IDUs

Zacny, James P. --- University of Chicago
Behavioral Effects of Opioids in Volunteers

Zahniser, Nancy R. --- University of Colorado Health Sciences Center
Cocaine Sensitization and the Dopamine Transporter

Zarkin, Gary A. --- Research Triangle Institute
Benefits of Treatment Services

Review Activities

Staff Development

In January 1999, Drs. Teresa Levitin, and William C. Grace presented at the NIH Peer Review Oversight Group to

discuss a model for web based training of reviewers. This training model was developed in conjunction with Drs. Marina Volkov and Susan Coyle of OEPR, and the web pages are currently under construction.

In March 1999, Dr. Mark Swieter, Scientific Review Administrator, completed reviews for applications for the Human Brain Project, a government-wide initiative designed to encourage and support investigator-initiated neuroinformatics research that will lead to new digital and electronic tools for all domains of brain and behavioral research reflecting normal and disease states across the lifespan. Participating agencies include 10 institutes of the NIH (including NIDA), the National Library of Medicine, the Fogarty International Center, the National Science Foundation, the National Aeronautics and Space Administration, the Office of Naval Research, and the Department of Energy.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****May, 1999**

Congressional Affairs

Hearings**National Institutes of Health Appropriations Hearings**

NIH officials testified in late February and early March 1999 before both the House and Senate Appropriations Subcommittees on Labor, Health and Human Services, Education and Related Agencies. On February 23, 1999, Dr. Harold Varmus, Director, NIH, accompanied by all of the NIH Institute Directors, appeared with Secretary Shalala at a hearing before the Senate Appropriations Subcommittee (Senator Specter, R-PA, Chair). The following day, Dr. Varmus testified before the Labor, Health and Human Services, Education and Related Agencies Subcommittee (Chairman John Porter, R-III) of the House Appropriations Committee.

NIDA Appropriations Hearing

On March 2, 1999, Dr. Alan I. Leshner, Director, NIDA, testified before the House Subcommittee on Labor, Health and Human Services, Education and Related Agencies, to discuss the Institute's FY 2000 non-AIDS budget request and to provide information on NIDA's ongoing and planned research activities. The FY 2000 budget request for NIDA is \$429.2 million, an increase of \$10.3 million (2.4%) above the FY 1999 appropriation. Including the estimated allocation for AIDS in the President's budget request, the total FY 2000 requested funding for NIDA would be \$622.8 million, an increase of \$14.6 million over the FY 1999 appropriation. Funds for NIDA efforts in AIDS research are included within the Office of AIDS Research budget request.

Dr. Leshner reported that NIDA has had another year filled with major scientific advances that directly benefit the citizens of this Nation, most particularly by enhancing drug addiction treatment. He explained that years of research discoveries brought to us through the use of advanced technologies, coupled with the generous appropriations that NIDA received last fiscal year are enabling the Institute to accelerate establishment of its much-needed National Drug Abuse Treatment Clinical Trials Network. This Network will serve as both the infrastructure for testing science-based treatments in diverse patient and treatment settings and as the mechanism for promoting the rapid translation of new science-based treatment components into practice. Dr. Leshner also described some of the significant discoveries and advances that are impacting the approach to addiction research. He discussed two technologies in particular - molecular genetics and brain imaging. In response to questions, Dr. Leshner described "NIDA Goes to School" - a science-based drug abuse education program aimed at middle school students. The program is available on NIDA's website.

Hearing on "Date Rape Drugs"

On March 11, the Oversight and Investigations Subcommittee (Chairman Fred Upton, R-MI) of the House Commerce

Committee held a hearing on "date rape" drugs, specifically including GHB (and its precursor GBL), Ketamine, and Rohypnol and their abuse. The subcommittee pointed out that GHB, GBL and Ketamine are currently not regulated under the Federal Controlled Substances Act, and indicated that it will study whether the federal government is taking enough action to combat the use of date rape drugs.

Dr. Stephen Zukin, Director, Division of Clinical and Services Research, NIDA, testified about what science has come to show about GHB. Other federal witnesses included Nicholas Reuter - Associate Director, FDA; Terrance W. Woodworth, DEA; Patricia Maher - DoJ.

Oversight Hearing on Efforts to Prevent and Treat Drug Abuse

On March 18, 1999, the House Government Reform Subcommittee on Criminal Justice, Drug Policy, and Human Resources, chaired by Representative John Mica (R-FL), held a hearing entitled, "Oversight of Agency Efforts to Prevent and Treat Drug Abuse." Mr. Richard Millstein, Deputy Director, NIDA, testified about research on prevention and treatment of drug abuse. Other witnesses included Daniel Schechter, Office of National Drug Control Policy; Joseph Autry III, SAMHSA; and Vicki Verdeyen, U.S. Department of Justice.

In his opening statement Representative Mica expressed his belief that "we cannot tackle the problems of drug abuse and the concurrent social problems, crime, and significant costs to our country, without an approach that addresses simultaneously education, treatment, prevention, enforcement, interdiction and eradication." He said the hearing was intended to focus on several critical elements of this effort, and expressed concern that 136 Floridians died from heroin overdoses in 1997, up from 84 in 1995, and that from 1991 to 1996 the proportion of the nation's 8th graders who said they had tried heroin had doubled.

Much of the hearing focused on the ONDCP 1999 National Drug Control Strategy, efforts to deal with the drug problem in the nation's prisons, and the recently released IOM report regarding the medicinal uses of marijuana. Most of the questioning, therefore, was addressed to the ONDCP witness.

In his oral remarks Mr. Millstein explained that science shows that drug abuse is a preventable behavior and drug addiction is in fact a treatable disease. Addiction is a chronic illness, similar to other chronic diseases like asthma, hypertension, and diabetes that have major medications and behavioral compliance issues, and are characterized for many people by occasional relapses. Mr. Millstein described NIDA's National Drug Abuse Treatment Clinical Trials Network as a major effort to move research into real-life settings. He said, "Ultimately, our best treatment is prevention." Mr. Millstein also emphasized the importance of a strong science education program to ensure that the nation's youth have the necessary information to make healthy lifestyle choices. He concluded that a comprehensive public health approach is needed that includes extensive education and prevention efforts, adequate treatment and aftercare services, and research.

Oversight Hearing on the ONDCP Youth Anti-Drug Media Campaign

On March 25, 1999, Dr. Alan I. Leshner, Director, NIDA, testified before the House Appropriations Subcommittee on Treasury, Postal Service, and General Government, Representative Jim Kolbe (R-AZ), Chairman, at an oversight hearing on ONDCP's Youth Anti-Drug Media Campaign. Also testifying were General Barry McCaffrey, Director, ONDCP; and James Burke, Chairman, Partnership for a Drug-Free America.

In his oral remarks, Dr. Leshner briefly described the role of NIDA in the ONDCP campaign, pointing out that research supported by the Institute played a significant role in developing the overall campaign design. He described the effort as the first science-based anti-drug media campaign. The NIDA-supported evaluation of Phase III of the campaign, aimed at determining the effectiveness of the campaign in changing attitudes and behaviors with respect to drug abuse, will begin at the end of the summer. This evaluation, he explained, will consist of three major data collection activities: (1) "The National Survey of Parents & Youth," which will provide data at six-month intervals regarding the nation's reaction to the campaign over four years; (2) "The Longitudinal Community Surveys of Parents & Youth," which will provide information about the impact of the campaign at the community level; and (3) an analysis of current long-term national monitoring mechanisms of drug use which will be compared with the information gained from the two new activities above.

Science-Based Approaches to Preventing and Treating Heroin Abuse and Addiction

March 30, 1999 -- At the request of Senator Pete Domenici (R-NM), Dr. Timothy Condon, Associate Director, NIDA, accompanied by Ana Anders, Senior Advisor on Special Populations, testified at a field hearing in New Mexico. The hearing focused on the problem of black tar heroin in northern New Mexico, which recently has been associated with 44 overdose deaths.

Dr. Condon testified about what science is teaching us about drug abuse and addiction, and heroin addiction in particular. He said that while drug abuse brings in its wake a myriad of health, social and economic problems, the good news is that we do have a strong research base that communities can call upon in their efforts to combat drug abuse and addiction. He provided an overview of the science of heroin describing its effects on brain function and the manifestation of these brain changes in development of tolerance and physical dependence. He emphasized that research has shown that integrating medication, such as methadone and LAAM, with behavioral-based therapies is likely to have the most success in treating heroin addiction. In an effort to give treatment providers another effective tool to combat heroin addiction, NIDA is working in collaboration with FDA to bring to market a new medication called buprenorphine. Buprenorphine would not replace methadone or LAAM but would be another component or option for treatment providers. Dr. Condon then described the soon-to-be-launched National Drug Abuse Treatment Clinical Trials Network that will test new behavioral and pharmacological therapies which we hope will be able to design treatments to meet the specific needs of special populations. He concluded by describing the many tools NIDA has made available for the public specifically describing the science-based prevention guide, "Preventing Drug Use Among Children and Adolescents."

NOTE: Congressional testimony of NIDA witnesses are available at the NIDA website: <http://www.nida.nih.gov/>. Click on "What's New". You may also wish to visit the NIH website: <http://www.nih.gov/>. Legislative information is available under the Office of the Director, Office of Legislative Affairs and Analysis.

Congressional Briefings

NIDA staff participated in several briefings for congressional staff and Members. On March 25, 1999, Dr. Alan I. Leshner was the keynote speaker at a Congressional Briefing "From Bench to Trench: Research-Based Approaches to Treating Drug Abuse and Addiction in Real-Life Settings" sponsored by the College on Problems of Drug Dependence, Inc. Other speakers were Dr. Thomas McLellan, Ph.D., University of Pennsylvania and Dr. Patricia Ordorica, University of South Florida. Dr. Warren Bickel served as moderator. On March 12, 1999, at the request of Senator Carl Levin (D-MI), Dr. Leshner, and Dr. Frank Vocci, Director, Division of Medication Development, provided a briefing on the current status of research on anti-addiction medications for the Senator. In February and March 1999, Dr. James Cooper, DCSR, participated in two briefings for Oversight and Investigations Subcommittee staff of the House Commerce Committee on issues related to several so-called date rape drugs.

Bills of Interest

HR 88 - On January 6, 1999, Rep. George Brown, D-CA, introduced the "Treasury and General Government Appropriations Act, Amendment" which would repeal a requirement regarding data produced under Federal grants and agreements awarded to institutions of higher education, hospitals, and other nonprofit organizations. The bill responds to a growing concern in the research community about the provision's effect on the privacy of human research subjects, the potential for theft of intellectual property, and the potential administrative costs for granting agencies and grant recipients. The provision was included in the omnibus appropriations package last session without any discussion or hearings on the subject. HR 88 was referred to the House Committee on Government Reform.

HR 278 - On January 6, 1999, Rep. Sweeney (R-NY) introduced HR 278, the "Drug Research Restriction Provision." The bill would "prohibit federally sponsored research pertaining to the legalization of drugs." The bill was referred to the House Committee on Government Reform.

HR 626 - Feb. 8, 1999, Rep. Sanders (I-VT) introduced the Health Care Research and Development and Taxpayer Protection Act. It would require any federal agency or non-profit entity that undertakes Federally funded health care research and development, and is to convey or provide an exclusive right to use such research and development for a drug or other health care technology, to enter into a reasonable pricing agreement with the Secretary of HHS. The bill was referred to the House Committee on Commerce.

HR 837/S 465 - On February 24, 1999, Representative George Miller (D-CA) and Senator Paul Wellstone (D-MN) introduced, respectively, H.R. 837 and S. 465, the Mental Health Juvenile Justice Act, which contains a number of

provisions regarding access to mental health and substance abuse treatment programs and services for juveniles who come into contact with the juvenile justice system. Section 6 of the bill would establish a Federal Coordinating Council on Criminalization of Juveniles With Mental Disorders, to study and coordinate the criminal and juvenile justice and mental health and substance abuse activities of the Federal Government, and whose membership would include NIMH, as well as: the Office of the Secretary, HHS; the Office for Juvenile Justice and Delinquency Prevention; the Social Security Administration; the Department of Education; SAMHSA; and representatives from children's mental health advocacy groups. H.R. 837 was referred to the Committee on Education and the Workforce, the Committee on the Judiciary, and the Committee on Commerce. S. 465 was referred to the Committee on the Judiciary.

HR 1065 - On March 10, 1999, Representative Stupak (D-MI) introduced H.R. 1065, "The Date Rape Prevention Act of 1999," which would require the Attorney General to add to schedule III of the Controlled Substance Act the "date rape" drugs ketamine hydrochloride (ketamine) and gamma hydroxybutyrate (GHB). The bill also provides for additional penalties (the same as schedule I or II drugs), and requires the Attorney General to establish a program to provide materials to young people in high school and college with education about the use of controlled substances in the furtherance of rape and sexual assault. H.R. 1065 was referred to the House Committees on Commerce, and on the Judiciary.

SR 47 - On February 12, 1999, Senator Frank H. Murkowski (R-AK) introduced SR 47, to designate the week of March 21 through March 27, 1999, as "National Inhalants and Poisons Awareness Week." The resolution encouraged parents to learn about, and discuss with their children, the dangers of inhalant abuse. The resolution was agreed to in the Senate on March 18.

S 324 - On January 28 Senator Hatch (R-OR), with Senators Levin (D-MI) and Moynihan (D-NY) introduced S 324 "The Drug Addiction Treatment Act of 1999". The bill amends the Controlled Substances Act with respect to registration requirements for practitioners who dispense narcotic drugs in schedule IV or V for maintenance treatment or detoxification treatment. The bill was referred to the Committee on the Judiciary. Sponsors of the bill indicate that it would allow qualified physicians to prescribe schedule IV and V anti-addiction medications in physicians' offices without an additional DEA registration if certain conditions are met. These conditions include certification by participating physicians that they are: licensed under state law; have the training and experience to treat opiate-dependent patients; have the capacity to refer patients to counseling and other ancillary services; and they will not treat more than 20 patients in an office setting unless the Secretary HHS adjusts that number. Senator Levin said "This will allow for a promising new drug, buprenorphine, to be used in the treatment of opiate addiction in physicians' offices."

S 326 - On March 18, 1999, the Senate Committee on Health, Education, Labor and Pensions [Senator Jeffords (R-VT), Chairman] approved 10-8 the "Patients Bill of Rights Act" which would provide new patient protections under group health plans. In addition to patient protection provisions, the bill contains provisions regarding: individual rights with respect to access to personal medical information; prohibiting genetic discrimination in health insurance; reauthorizing and renaming the Agency for Health Care Policy and Research (AHCPHR) as the Agency for Healthcare Research and Quality; and permitting contributions towards Medical Savings Accounts through the Federal Employees Health Benefits Program (FEHBP). During the mark-up, an amendment offered by Senator William Frist (R-TN) was approved that would require the Institute of Medicine to examine the use of clinical trials. In addition, Title II, regarding individual rights with respect to access to personal medical information, was deleted from the reported bill.

S 423 - On February 11, 1999, Senator John McCain (R-AZ) introduced "The Addiction Free Treatment Act of 1999." The bill would (in part) restrict Medicaid reimbursements and funding through the Substance Abuse and Mental Health Services Administration for methadone and LAAM maintenance programs; require that methadone or LAAM treatment programs have as their primary objective the elimination of drug addiction, including "addiction" to methadone or LAAM; require that methadone and LAAM maintenance programs be limited to 6 months; require that patients be subject to frequent drug testing for all narcotics; terminate methadone or LAAM treatment for any patient who tests positive for any other illegal narcotic during the duration of their methadone or LAAM treatment; and require the Director of NIDA to complete a study within three years of enactment of the Act concerning "(1) the methods and effectiveness of nonpharmacological heroin rehabilitation programs; and (2) the methods and effectiveness of methadone-to-abstinence programs." The bill was referred to the Senate Committee on Finance.

S 562/HR 988 - On March 8, 1999, Senator Tom Harkin (D-IA) introduced "The Comprehensive Methamphetamine Abuse Reduction Act," which would provide for a comprehensive, coordinated effort to combat methamphetamine abuse (MA). Research provisions would amend NIDA authorities to permit its Director to make grants to expand interdisciplinary research and clinical trials relating to MA and addiction and other biomedical, behavioral and social issues relevant to such abuse. This bill is the companion to H.R. 988, introduced by Representative Leonard Boswell (D-IA) on March 4, 1999. S. 562 was referred to the Senate Committee on the Judiciary.

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National Institute on Drug Abuse**Director's Report to the National Advisory Council on Drug Abuse****May, 1999**

International Activities

On March 22-23, 1999, Dr. Alan Leshner hosted an official delegation from The Netherlands representing the Committee of the Dutch Program on Addiction (Netherlands Organisation for Scientific Research, and Health and Development Council). The purpose of the visit was to exchange information on addiction research, particularly in the areas of epidemiological surveillance, prevention and treatment, and to explore possibilities for research collaboration with NIDA. NIDA staff presenters included Dr. Kathleen Etz, Prevention Research Branch, DEPR; Dr. Jack Blaine, Treatment Research Branch, DCSR; Nicholas Kozel, DEPR; and Dr. Bennett Fletcher, Services Research Branch, DCSR. The meeting resulted in agreement to establish research cooperation in areas of mutual interest, and to meet again in The Netherlands in October to formalize plans for the cooperation and to participate in a joint scientific symposium.

On February 23, 1999, the review committee for the NIDA Hubert H. Humphrey Drug Abuse Research Fellowship met to select Fellows for the 1999-2000 academic year. Four prospective Fellows Teodora Ciolompea (Romania), Tatiana Kitkina (Russia), Evodia Mokoko (South Africa) and Sergiy Dvoryak (Ukraine) were selected to participate in the program at The Johns Hopkins University. This NIDA-supported component of the Humphrey Program includes a four- to six-week professional affiliation with a NIDA grantee to design a research proposal for implementation in the Fellow's home country after return.

In late February, NIDA's International Program, Office of Science Policy and Communications, arranged an orientation visit to the Institute for 1998-1999 INVEST Research Fellows Dr. You Wan (China) and Dr. Neo Morojele (South Africa). Also invited were AIDS International Training and Research Program (AITRP) Fellows Dr. Ola Borodkina and Roman Dyatlov, both of Russia. The orientation included a welcome from NIDA Director Dr. Alan Leshner and presentations by NIDA staff about grant application requirements, funding and proposal preparation. The group also paid a visit to the NIDA Intramural Research Program in Baltimore to learn about the research being conducted there.

Mr. Nicholas J. Kozel, DEPR, participated in the regional meetings of the South African Community Epidemiology Network on Drug Abuse (SACENDU) on March 15-19, 1999 in Cape Town, Port Elizabeth, Durban and Johannesburg. SACENDU is sponsored by the Medical Research Council of South Africa and World Health Organization (WHO). SACENDU's mission is to develop a multi-city drug abuse surveillance program in the country based on epidemiologic and ethnographic data. Historically, the most serious substance abuse problems in South Africa have involved alcohol, cannabis and Mandrax. Recently, new drugs, especially crack cocaine and heroin, have become available, as well as LSD and ecstasy. Recent information also reveals an increase in drug abuse among youth and an increase in intravenous drug use. Based on the success of SACENDU over the past three years in implementing an effective drug abuse surveillance program in South Africa, the Medical Research Council has been notified that it will receive a grant from the European Union to transfer the epidemiology network technology to Southern African Developing Countries (SADC), including Namibia, Zimbabwe, Botswana, Lesotho, Zambia, Mozambique and Swaziland, with the objective of establishing a regional epidemiologic surveillance infrastructure.

Mr. Nicholas J. Kozel, DEPR, co-chaired a joint meeting of the East and South Asian Multi-City Epidemiology Work Group (AMCEWG) meeting held in Penang, Malaysia on November 9-12, 1998. The AMCEWG was established in 1990 and is composed of researchers from Kuala Lumpur, Manila, Bangkok, Yangon, Beijing, Hanoi, Taipei, Vientiane,

Dhaka, Colombo, Islamabad, and Madras. An Advance Report and a meeting Proceedings are produced annually describing the current status of drug abuse in the AMCEWG cities and emerging drugs of abuse. Heroin is the primary drug of abuse in both East and South Asian countries. Recent increases in opium abuse have been noted in East Asian countries, while buprenorphine continues its upward trend in South Asia. A major emerging drug problem throughout the East Asia is methamphetamine abuse. In addition, "ecstasy" has become firmly established as a "club drug" in East Asia and is making inroads as a drug of abuse in South Asia. The endemic level of abuse of benzodiazepines and inhalants continues throughout both South and East Asia. The AMCEWG project is jointly funded by the Association of South East Asian Nations and the Government of Malaysia and recently has received a grant from the United Nations International Drug Control Programme to expand its membership and data collection activities.

Mr. Nicholas J. Kozel, DEPR, was the recipient of a Fellowship from the Ministry of Health and Welfare of Japan. The Fellowship was arranged by the National Institute of Mental Health, Division of Drug Dependence and Psychotropic Drug Clinical Research of the National Center of Neurology and Psychiatry and was sponsored by the Society of Japanese Pharmacopoeia. The Fellowship took place on February 1-10, 1999, and involved information exchange, primarily through visits to drug abuse research, treatment and prevention offices for discussions with researchers and program officials about the current status of drug abuse in Japan. Discussions also focused on data development and establishment of a community based infrastructure for drug abuse epidemiologic surveillance.

On January 4, 1999, Dr. Elizabeth Robertson, PRB, DEPR, met with Mr. Gustavo Ascacibar from the Drug Enforcement Commission of Peru and Carmen Luisa Barrantes, the coordinator of demand reduction programs at the U.S. Embassy. Prevention programming in Peru and the United States was discussed.

On April 26-30, 1999, Drs. Robert Battjes and Bennett Fletcher, Division of Clinical and Services Research, participated in meetings of the NIH-World Health Organization Joint Project on Assessment of Disablements, held in Geneva Switzerland. Under this project, cross-cultural assessment instruments are being developed to measure the extent of disability and functional limitation resulting from alcohol, drug abuse, mental and physical disorders. Health services research pilot studies will be conducted to assess the utility and validity of the instruments in predicting service utilization and clinician-assessed needs. A methodology will also be developed to estimate disability weights that can be used in the calculation of Disability Adjusted Life Years (DALYS) for selected disorders.

Dr. Amy Newman, IRP, presented the Sato Memorial International Award Address entitled "Novel Probes for the Dopamine Transporter" at the 119th Annual Meeting of the Pharmaceutical Society of Japan held in March 1999.

In collaboration with Drs. Tangui Maurice and Alain Privat at the Institut National de la Santé et de la Recherche Médicale in Montpellier, France, Drs. Tsung-Ping Su and Steven Goldberg, NIDA IRP, are studying the effects of methamphetamine self-administration on the regulation of type 1 sigma receptors which have been shown to be related to learning and memory, and perhaps drug-seeking behavior, in animals.

On April 9, 1999, Ms. Doris Olmedo, Deputy Director, Press Administration, Ministry of the Presidency of Panama, visited NIDA to learn about the Institute's research portfolio and publications on prevention and treatment of drug abuse.

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National Institute on Drug Abuse
Director's Report to the National Advisory Council on Drug Abuse
May, 1999

Meetings/Conferences

"Neurotrophic Factors: Tools for Modifying the Brain" was held at Lister Hill Auditorium, NIH campus, January 6-7, 1999. The meeting, organized by Dr. Nancy Pilotte, DBR, focused on the newly appreciated novel growth factors, the neurotrophins, which can serve to promote neural growth, and their possible role in brains chronically exposed to drugs of abuse.

NIDA's Behavioral Science Working Group co-hosted, with the Society for Research on Nicotine and Tobacco, a special plenary symposium titled **"Highlighting New Investigators in Nicotine and Tobacco Research"** at the annual meeting of the Society for Research on Nicotine and Tobacco in San Diego, California on Saturday March 6, 1999. Participants were: Stephen Heishman, NIDA; Jack Henningfield, Pinney Associates and the Johns Hopkins School of Medicine; Neil Grunberg, The Uniformed Services University of the Health Sciences; Dorothy Hatsukami, University of Minnesota; Maxine Stitzer, The Johns Hopkins University School of Medicine; and, Jaylan S. Turkkan, NIDA. New investigators that were highlighted in the symposium were: Beth C. Bock, Brown University School of Medicine; Jon D. Kassel, University of Illinois at Chicago; and James W. Shaw, The University of Arizona. This symposium is one of seven national events sponsored by the Behavioral Science Working Group titled "Early Career Pathways: Opportunities for Behavioral Researchers". Upcoming symposia will be at meetings of the American Psychological Society, CPDD, Society for Prevention Research, AIDS Impact, and the Society for Neuroscience.

On March 9, 1999, NIDA and the Entertainment Industries Council (EIC) held an event in Beverly Hills, CA during which the **Third Annual PRISM Awards** were presented, spotlighting outstanding efforts of the entertainment industry to accurately depict drug use and addiction in entertainment products.

This year, NIDA staff took on the responsibility of coordinating the NIH neuroscience event during Brain Awareness Week. **"Neuroimaging: Glimpses into the Working Brain"** took place on March 16, 1999, with a morning scientific session and an evening presentation geared to the general public. Eleven Institutes at NIH were cosponsors of the event.

A technical assistance meeting of grantees funded under the **NIH Consortium on Domestic Violence** administered by NIDA (Dr. Coryl Jones, ERB/DEPR) was held April 26-27, 1999, in Washington, DC, to discuss progress, findings, and problems in this type of research. Other investigators with studies on violence against women and within the family funded by participating Institutes were also invited. Dr. Bernie Auchter, NIJ, chaired the meeting.

Buprenorphine: A New Option for the Treatment of Opioid Addiction for the Practicing Physician was held on April 30, 1999 at the Marriott Marquis Hotel, New York, New York, in conjunction with the annual Medical-Scientific Conference of the American Society of Addiction Medicine. This NIDA/ASAM day-long symposium was co-chaired by Dr. Frank Vocci, Director, Medication Development Division in NIDA, and Dr. Donald Wesson, Chair of the ASAM Medications Development Committee. This meeting was planned by Drs. Tai, Blaine, and Czechowicz and NIDA's Treatment Research Workgroup. The symposium presented scientific information on the pharmacology and mechanism of action of buprenorphine; results from clinical trials of buprenorphine and from studies integrating this pharmacotherapy with a behavioral therapy to maximize treatment effectiveness; and addressed issues related to the treatment of women, polydrug abusers, and individuals with medical and/or psychiatric comorbidity. Research on office-based treatment for opioid addiction was also presented and discussed.

NIDA held a Town Meeting in Atlanta, Georgia entitled "**Understanding Drug Abuse and Addiction: Myths versus Reality**" on May 6, 1999. NIDA Director Dr. Alan I. Leshner and NIDA researchers discussed ways that state policy makers, organizations, schools and communities can utilize the latest scientific research to assess state and local drug problems and tailor programs to meet these needs. As part of publicity/outreach for the May 5-6 Town Meeting in Atlanta, NIDA articles and information were featured in the April 27th edition of the City Hall Newspaper, City Beat, and 60,000 copies were distributed in the Atlanta area.

The Medications Development Division, in conjunction with the Food and Drug Administration, the College on Problems of Drug Dependence, the Society for Research on Nicotine and Tobacco, and the National Institute on Alcoholism and Alcohol Abuse sponsored a meeting on April 28-29, 1999 to discuss efficacy endpoints and outcomes for pharmacological treatments for cocaine, alcohol, and nicotine dependence.

Mr. Richard A. Millstein, NIDA Deputy Director, served on an expert panel that provided advice to the University of Delaware Center for Drug and Alcohol Studies on its RWJ award to develop an illicit drug surveillance system, April 8-9, 1999, Washington, D.C.

Mr. Richard Millstein attended the annual meeting of the Council on Foundations and sessions of Grantmakers in Health, Funders Against AIDS, and children and family interest groups to begin to explore potential NIDA-community-foundation collaborative activities, April 18-21, 1999, New Orleans, LA.

On April 27, 1999, accompanied by Ms. Ana Anders, NIDA Senior Advisor on Special Populations, Mr. Richard Millstein held a followup meeting with Dr. Carlos Ugarte, Coordinator of the NIH Hispanic Communications Initiative, NIH Office of the Director, to share NIDA activities and interests and to consider further developmental activities. As a next step Mr. Millstein has invited Dr. Ugarte to meet with NIDA senior staff on May 27, 1999.

Mr. Richard Millstein presented "The Science of Addiction: Research and Public Health Perspectives" at the University of Maryland School of Law Conference on "Substance Abuse, Families and the Courts: Legal and Public Health Challenges," May 14, 1999, Baltimore, MD.

On January 11, 1999, Lula Beatty presented a session on drug abuse research opportunities for participants in the NIH Extramural Associates Program.

On January 13, 1999, Lula Beatty conducted a faculty development seminar on research development for the School of Arts and Sciences at Coppin State College in Baltimore, Maryland.

On March 15, 1999, Lula Beatty presented a class lecture to foreign service majors on Drug Abuse and Minority Youth at Georgetown University.

On March 17, 1999, Lula Beatty presented the inaugural lecture, "Preventing Drug Abuse in Black Youth," for the Henry Cornwell Distinguished Lecture Series at Lincoln University in Oxford, Pennsylvania.

As a liaison from the Division of Women, American Psychological Association (APA), Lula Beatty attended the meeting of the Committee on Women during the APA's governance board meetings held March 20-22, 1999. She made a presentation on drug abuse research and women and research opportunities at NIDA to the committee.

On January 7-8, 1999, Ana Anders, Senior Advisor on Special Populations, Special Populations Office, met with a subcommittee of the Hispano/Latino Researchers and Scholars Work Group (HLRSWG) to plan for the upcoming HLRSWG annual meeting.

As a representative of NIDA, On April 17, 1999, Ana Anders participated in a town meeting in Espanola, New Mexico, called by Senator Pete Domenici. At the meeting, the town's black tar heroin epidemic was discussed.

As a representative of NIDA, Ana Anders has attended ongoing meetings with multiple federal agencies hosted by ONDCP. They have met to plan the Second U.S./Mexico Demand Reduction Binational Conference, which will take place in Tijuana, Mexico in June, 1999.

As a representative of the Special Populations Office, Ana Anders attended the "Substance Abuse in Primary Care Settings: Treating Hispanic Patients" conference in New York, New York on April 17, 1999. The conference was sponsored by the Interamerican College of Physicians & Surgeons (ICPS) in collaboration with the Center for Substance Abuse Treatment, SAMHSA, the National Institute on Drug Abuse, The Bureau of Primary Health Care, HRSA and the Office of Minority Health, DHHS.

On April 9, 1999, Ana Anders met with representatives from NIMH, SAMHSA, CDC, HRSA and OMH to brainstorm on

developing a project on Hispanic health issues that are common to the agencies. The project is aimed at closing the gap on the disparity of health among Hispanics.

Ana Anders presented NIDA's mission, programs for special populations and initiatives, particularly the Hispanic Initiative, to the National Boricua Latino Health Organization (NBLHO) at their annual conference held in Philadelphia on March 27, 1999.

Dr. Frank Vocci, Director, Medications Development Division, was a discussant on Therapeutic Drug Development at the Fifth Office of National Drug Control Policy International Technology Symposium held in Washington, D.C. on March 9, 1999.

Dr. Frank Vocci, MDD presented a talk entitled "Development of Medications for Opiate Dependence" at the 1999 American Society for Clinical Pharmacology and Therapeutics meeting, San Antonio, Texas, March 19, 1999.

Dr. Frank Vocci was a co-Chair, along with Dr. London of the IRP, of a neuroscience breakout session of the NIH Biomarkers meeting entitled "Biomarkers and Surrogate Endpoints: Advancing Clinical Research and Applications" on April 15-16, 1999. The session featured presentations on cue-induced and drug induced craving for cocaine, the role of endogenous opioid receptor systems in the response to naltrexone in treatment of alcoholism, the role of computerized cognitive testing in drug development, markers for alcohol consumption, markers of vulnerability to alcohol abuse, and integration of data domains into an index biomarker.

Dr. Teresa Levitin, Director, OEPR, presented at the 1999 Society of Research in Child Development biennial meeting held in Albuquerque, NM in April 1999. She participated in a symposium for new investigators, "How to Create Your Research Career: Mentoring, Networking, and Grant Writing". She also participated in a symposium on behavioral science and child and adolescent research at NIDA.

Mr. Richard Harrison, Chief of the Contracts Review Branch, OEPR, participated in a meeting of an interagency group coordinated by the Indian Health Service to assist the Department of Justice (DOJ) in an initiative to address crime issues affecting Native American Tribes. The DOJ is particularly interested in providing assistance to Tribes to help them deal with issues such as alcohol abuse, drug abuse, child abuse, domestic violence and treatment issues.

Dr. Arthur MacNeill Horton, Jr. attended the Society for Research in Child Development meeting in Albuquerque, New Mexico, April 15-18, 1999 and co-chaired two sessions: "How to Create Your Research Career: Mentoring, Networking, and Grant Writing" and "Behavioral Science and Child and Adolescent Research at NIDA."

Dr. Peter Delany, Deputy Chief, Services Research Branch, co-chaired a meeting entitled "HIV/AIDS Services in Drug Abuse Treatment Settings: Expanding Research and Practice," held in Bethesda March 25-26, 1999. This meeting, co-sponsored by NIDA and the National Developmental Research Institutes, Inc., was attended by researchers, constituent representatives, and representatives from other Federal agencies. Participants heard brief presentations on the dimensions of the problem confronting drug treatment programs, organizational and systems issues, advances in interventions, and the needs of special populations. Materials from this meeting will be developed for a proceedings paper to be placed on the Resource Center for Health Services Research Website.

Drs. Peter Delany and Jerry Flanzer, SRB, DCSR represented NIDA at the Annual Program Meeting of the Council of Social Work Education in San Francisco, March 10-14, 1999. Drs. Delany and Flanzer also led workshop groups on NIDA health services research opportunities for junior faculty and doctoral students (co-sponsored by the Institute for Advancement of Social Work Research), and met with the Steering Committee of the Alcohol, Tobacco and Other Drug Section (ATOD) of the National Association of Social Workers.

Dionne J. Jones, Ph.D., CRB/DEPR, gave a presentation on "Research Synthesis and Meta-Analysis of the NIDA's Community-Based AIDS Research Program," at a Workshop on Research Syntheses and Meta-Analyses co-sponsored by the National Institute of Mental Health, Centers for Disease Control and Prevention, and the National Institute on Drug Abuse, on February 19, 1999, in Rockville, MD. Dr. William J. Bukoski, OD/DEPR, was appointed to the Evaluation Guidance Committee for the Center for Substance Abuse Prevention's (CSAP) National Cross-site Evaluation of State Incentive Grants (SIG), a three year \$171 million dollar CSAP discretionary grant program in 19 States designed to promote the adoption of science-based prevention. The committee will meet several times a year to discuss research issues related to the design and implementation of the evaluation that is being conducted under a contract to COSMOS Corporation. The first meeting of the Committee was March 10, 1999.

Dr. William J. Bukoski, OD/DEPR, was appointed to the National Advisory Panel of the Centers for the Application of Prevention Technologies (CAPT), a three year \$18 million dollar program sponsored by the Center for Substance Abuse Prevention. The first meeting of the CAPT Advisory Panel was held on March 17, 1999. The purpose of the panel is to provide input to the Centers in their efforts to bridge the gap between prevention science and practice

through training, technology transfer, and technical assistance.

On March 18, 1999, Dr. William J. Bukoski, OD/DEPR, participated in a panel presentation on the topic of "A Multidisciplinary Approach to Substance Abuse," at the 16th Annual National Preventive Medicine Meeting sponsored by the American College of Preventive Medicine and the Association of Teachers of Preventive Medicine. On the panel with Dr. Bukoski were Tom Vischi, DHHS; Janet Chinconie, Policy Analyst, Department of Justice; and, Steve England, M.D., Presidential Fellow, Department of Education. The presentation summarized key points contained in a paper on prevention science that was developed by an inter-departmental Federal work group convened by DHHS as part of the Secretarial Initiative on Youth Substance Abuse Prevention. The paper is titled: "Science-based Substance Abuse Prevention," and summarizes the characteristics and principles of science-based substance abuse prevention programs and policies.

Dr. Naimah Weinberg, DEPR, presented an overview of risk factors for adolescent substance abuse, at a conference sponsored by the National Center on Addiction and Substance Abuse and the National Center for Learning Disabilities, in New York City on February 1, 1999.

Dr. Coryl Jones, ERB/DEPR served on the DHHS panel and editorial for the report mandated by the Adoption and Safe Families Act (ASFA, P.L. 105-89) to "describe the extent and scope of the problem of substance abuse in the child welfare population," services provided, outcomes, and recommendations. In the report, just released, most studies found that half to three-quarters of substantiated child abuse and neglect reports involve substance abuse. Half of drug-related cases involve children under 5 years of age. Children of drug dependent parents were identified as having an 8-fold increased risk of becoming drug abusers themselves thus are a high priority for preventive interventions. U.S. Department of Health and Human Services, Blending Perspectives and Building Common Ground, Report to Congress on Substance Abuse and Child Protection. Washington, D.C.: U.S. Government Printing Office, 1999. Available from the National Clearinghouse on Child Abuse and Neglect Information, 1-800-FYI-3366 and accessed electronically at either www.aspe.os.dhhs.gov or www.acf.dhhs.gov/programs/cb/.

Dr. Elizabeth Robertson, PRB, DEPR, made a presentation on drug abuse in rural America at the Drug Enforcement Administration, Mid-Size Cities Conference on February 22, 1999 in Herndon, VA. Jeffrey Merrill and Dr. Elizabeth Robertson, PRB, DEPR, co-hosted a meeting on the Prevention Services Research agenda, at the Doubletree Hotel on March 17, 1999.

Dr. Elizabeth Robertson, PRB, DEPR, made a presentation on research-based family prevention interventions at CSAPs National Prevention Congress on March 23, 1999.

Dr. Elizabeth Robertson, DEPR, represented NIDA at the Prevention Roundtable on March 2, 1999. The Roundtable coordinates prevention activities across federal agencies.

Dr. Coryl Jones, ERB/DEPR gave a presentation and workshop on career development opportunities in drug abuse research at the NIH Child Abuse and Neglect Technical Workshop, February 17-18, 1999, in Bethesda, MD. The 40 investigators who attended seek to focus their work on child abuse and neglect through research training and career development (K awards) under a new NIH initiative to assist investigators conduct multi-disciplinary, clinically-relevant research on basic biological, behavioral, and social aspects of child and adolescent abuse and neglect. Participating institutes include NIDA, NIMH, NICHD, NIAAA, and NINDS.

Dionne J. Jones, Ph.D., of CRB/DEPR, gave a presentation on "Research Synthesis and Meta-Analysis of the NIDA's Community-Based AIDS Research Program," at a Workshop on Research Syntheses and Meta-Analyses co-sponsored by the National Institute of Mental Health, Centers for Disease Control and Prevention, and the National Institute on Drug Abuse, on February 19, 1999, in Rockville, MD.

Jacques Normand, Ph.D., of CRB/DEPR, was a discussant in the symposium, "Beyond Drug-Testing: Recent Innovations in Workplace Substance Use Prevention," an APA-NIOSH Interdisciplinary Conference on Work, Stress, and Health, held in Baltimore, March 13, 1999.

Dr. Ro Nemeth-Coslett, DEPR, organized a meeting at the request of National Association of Children of Alcoholics (NACoA) to provide information on children of drug users for a fact sheet sponsored by NACoA. Drs. Kathy Etz and Elizabeth Robertson, DEPR, Dr. Vince Smeriglio, CAMCODA, and Dr. Cathy Cordigan, NACoA, also participated in the meeting held on March 3, 1999.

Dr. Kenzie Preston, IRP, presented "Urine and Sweat Monitoring of Illicit Opiate Use" at the annual scientific meeting of the American Society for Clinical Pharmacology and Therapeutics in San Antonio, Texas, in March 1999.

Dr. David A. Gorelick, Chief, Pharmacotherapy Section, IRP, organized and chaired a symposium entitled "Update on

Treatment of Stimulant Abuse" at the American Psychiatric Association annual meeting, Washington, D.C., May 20, 1999.

Dr. Monique Ernst, IRP, presented "Functional Imaging in Neuropsychiatric Disorders" at NIMH, Jan. 11, 1999, Bethesda, MD.

Dr. Edythe D. London, IRP, presented "Common Problems in Brain Imaging Studies of Drug Abuse" at the Neurobiology of Addiction Conference, Los Angeles, CA, Jan. 12-13, 1999.

Dr. Monique Ernst, IRP, presented "The Dopaminergic Neurotransmitter System in ADHD" at the University of California, Irvine Grand Rounds, Jan. 13, 1999, Irvine, CA.

Dr. Edythe D. London, IRP, participated in a panel entitled "Novel Approaches to Smoking Cessation: Different Smokes for Different Folks" at the 32nd Annual Winter Conference on Brain Research, Snowmass, CO, Jan. 22-30, 1999.

Dr. Monique Ernst, IRP, presented "Neurobiology of Attention-Deficit Hyperactivity Disorder" at Beth Israel Medical Center Grand Rounds, New York, NY, Feb. 11, 1999.

Dr. Monique Ernst, IRP, presented "Attention-Deficit Hyperactivity Disorder, from Behavior to Brain" at the Hopital Robert Debre Ground Rounds, Paris, France, Feb. 18, 1999.

Dr. Monique Ernst, IRP, presented a general lecture on attention-deficit/hyperactivity disorder at Children's National Medical Center, Department of Psychiatry and Behavioral Sciences Grand Rounds, Washington, DC, Mar. 3, 1999.

Dr. Monique Ernst, IRP, presented "Nicotine Effects on Cerebral Blood Flow during a Working Memory Task" at the Society for Research on Nicotine and Tobacco (SRNT) Meeting, San Diego, CA, Mar. 7-8, 1999.

Dr. D. Bruce Vaupel, IRP, presented "Imaging Nicotinic Acetylcholine Receptors Using 5-[123/125I]Iodo-A-85380" at the Society for Research on Nicotine and Tobacco (SRNT) Meeting, San Diego, CA, Mar. 7-9, 1999.

Dr. Edythe D. London, IRP, presented "Imaging Technologies Reveal Persistent Abnormalities in the Brains of Substance Abusers" at the 1999 Office of National Drug Control Policy International Technology Symposium, Washington, DC, Mar. 8, 1999.

Dr. Monique Ernst, IRP, presented "The Dopaminergic Hypothesis of Attention-Deficit/Hyperactivity Disorder" at the University of Southern California School of Medicine Grand Rounds, Los Angeles, CA, Mar. 9, 1999.

Dr. Steven Grant, DCSR, presented "Imaging Drug Abuse" at Neuroscience Day 1999, Maryland Psychiatric Research Center and Intramural Research Program of the National Institute on Drug Abuse, Baltimore, MD, Mar. 23, 1999.

Dr. D. Bruce Vaupel, IRP, presented "Imaging Nicotinic Acetylcholine Receptors" at Neuroscience Day 1999, Maryland Psychiatric Research Center and Intramural Research Program of the National Institute on Drug Abuse, Baltimore, MD, Mar. 23, 1999.

Dr. Monique Ernst, IRP, presented "ADHD's Odyssey through 10 Years of PET" at NIH's PET Interest Group Seminar Series, Bethesda, MD, Apr. 9, 1999.

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Media and Education Activities

Awards

The NIDA Goes To School toolbox of materials was a Finalist in the Astrid Awards given by MerComm, Inc., honoring outstanding design communications. The toolbox contained many materials written specifically for students in grades 5 through 9, including the Mind Over Matter magazines featuring the cartoon adventures of Sara Bellum, a girl who explores the brain's response to particular drugs and introduces key concepts in neuroscience, and ATOD-TV, an interactive CD-ROM, featuring information on drugs of abuse in a variety of television show formats. Other materials in the toolbox included NIDA publications and fact sheets.

PRIDE World Conference, April 8-9. Dr. Leshner appeared as a keynote speaker at the PRIDE conference in Cincinnati. He also spoke to Cincinnati-based counselors, medical directors, and community-based physicians at the Hamilton County Alcohol & Addiction Services Center. During an evening awards gala, Dr. Leshner was presented with PRIDE's Network to Freedom Award.

As a result of these appearances, Dr. Leshner was quoted in an April 8 article in The Cincinnati Post, which also highlighted the NIDA Goes to School Material. In addition, the ABC TV affiliate, WKRC, interviewed and taped Dr. Leshner for a piece on inhalant abuse among young people, which aired April 29.

Press Releases

March 3, 1999 **Advances in Imaging and Understanding the Human Brain Featured in NIH Commemoration of Brain Awareness Week.** Noninvasive technology has become the scientist's window into the brain and how it functions. To help commemorate Brain Awareness Week, NIH sponsored morning and evening symposia on March 16, showcasing what scientists are learning about the brain from neuroimaging advances. "Neuroimaging: Glimpses into the Working Brain," featured both the history and future of imaging technology.

March 16, 1999 **Higher Doses of Methadone Found to Be Safe and Effective.** Researchers have demonstrated that methadone can be used safely at dose levels higher than those often considered standard, and that the higher dosages significantly improve treatment outcomes. They also showed that addicts receiving even low doses of the medication are more likely to remain in a treatment program than those receiving no methadone.

March 22, 1999 **Researchers Discover Function for Brain's Marijuana-Like Compound.** Researchers, funded in part by NIDA, have discovered a function for a natural compound in the brain that is chemically similar to the active ingredient in marijuana. This finding may lead to the development of new medications for treating a wide variety of disorders. As a result, an article appeared in the *San Jose Mercury News*.

Media Advisories

January 13, 1999 **Ð NIDA Launches a Major Effort to Establish National Drug Abuse Treatment Clinical Trials Network.** NIDA has taken major steps forward in establishing a critically needed research infrastructure that will test and disseminate science-based addiction treatments in real life settings throughout the country by establishing the National Drug Abuse Treatment Clinical Trials Network. As a result, articles appeared in the AAAP Newsletter, the American Psychological Society Observer, and CADCA's Coalitions.

March 9, 1999 - **Miramax, NBC, CBS, & ABC Among Winners of PRISM Awards Which Champion Accurate Depiction of Drug Use In Movies & On TV.** The Third Annual PRISM Awards, which spotlight outstanding efforts of the entertainment industry to accurately depict drug use and addiction in entertainment products, were presented at the Beverly Hills Hotel, Beverly Hills, CA. As a result, stories appeared on all TV Channels in LA, plus in USA Today, The Los Angeles Times, Daily Variety, The Hollywood Reporter, Substance Abuse Report, Alcoholism and Drug Abuse Weekly, and TV Guide On-Line's Daily Dish, and an Associated Press story ran in over 100 newspapers nationwide.

NIDA Exhibits Program

The following are meetings where NIDA exhibited its publications and program announcements over the past several months:

February 24-27, 1999 -- American Society of Neuroimaging

February 26-March 2, 1999 -- National Association of Secondary School Principals

March 9, 1999 -- PRISM Awards

March 18-21, 1999 -- Prevention '99 Scientific, Political and Social Priorities for the 21st Century

March 25-28, 1999 -- 47th Annual National Science Teachers Association

April 8-10, 1999 -- Parent Resource Institute for Drug Education

April 15-18, 1999 -- Society for Research in Child Development

April 17, 1999 -- Interamerican College of Physicians and Surgeons

April 1999 -- NIDA Mini-town Meeting

April 28-May 1, 1999 -- The Lonnie E. Mitchell National HBCU Substance Abuse Conference

April 29-May 2, 1999 -- 45th Annual Meeting of the American Society of Addiction Medicine

May 6, 1999 -- NIDA Town Meeting

May 15-20, 1999 -- American Psychiatric Association

May 22-28, 1999 -- International Society for Magnetic Resonance in Medicine

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Publications

Research Report Series: Cocaine Abuse and Addiction

NIH pub. No. 99-4166

This issue will explore what cocaine is like, how it is used, what the short- and long-term effects are, how cocaine abuse can affect pregnancy, and what treatment is available. A glossary and a resource list will help stimulate further study.

Epidemiologic Trends in Drug Abuse, Proceedings of the Community Epidemiology Work Group - Volume I: Highlights and Executive Summary - December 1998

NIH Pub. No. 99-4526

This report provides program administrators and officials with specific indicators and ethnographic information on current patterns and trends as well as emerging problems.

An Individual Drug Counseling Approach: Treating Cocaine Addiction

NIH Pub. No. 99-4380

This publication describes a specific behavioral model of counseling, which can be implemented in a wide range of different drug abuse treatment settings. It is a component of NIDA's Treatment Initiative one of the goals of which includes dissemination of behavioral and cognitive treatment approaches which have been proved effective through research to agencies and service providers in order to improve drug abuse treatment services and outcomes.

Videos**Treatment Solutions - Video**

NCADI DD110 (19 minutes)

NCADI DD111 (10 Minutes)

Viewer's Guide, NCADI DD110G

This is a 19-minute-long videotape, which describes the latest developments in treatment research. Expertly produced, and highly engaging, the program covers such issues as treatment medications and behavior modification techniques. It also stresses the benefits of drug abuse treatment, both to the patient and to the greater economy. A 10-minute version of Treatment Solutions is also available. A comprehensive viewer's guide to the videotape is enclosed.

Drug Abuse and Addiction: Bridging the Great Disconnect Between Myths and Realities - Video

NCADI VHS109

Viewer's Guide, VHS109G

A new videotape produced by NIDA shatters those myths in an entertaining and informative way. The 10-minute presentation employs high-tech computer-generated graphics and special effects. It shows, in easily understood terms, the dramatic changes in brain function occurring in drug abusers and addicts. A comprehensive viewer's guide

to the videotape is enclosed.

NIDA NOTES

NIDA NOTES, Vol. 13, Issue No. 5

NCADI NN0033

The lead story in this issue of NIDA NOTES reports on NIDA's Nicotine Conference. The Director discusses NIDA's health services research in conjunction with a report on a NIDA symposium on the subject. Another story covers an imaging study that has identified areas of the brain activated by cocaine. This issue also highlights NIDA's new Center on AIDS and Other Medical Consequences of Drug Abuse and the Institute's new Global Research Network on HIV Prevention in Drug-Using Populations.

NIDA NOTES, Vol. 13, Issue No. 6

NCADI NN0034

The front-page story and the Director's Column in this issue both highlight NIDA's Vulnerability to Addiction Initiative. Research on a gene variant that makes people less likely to become addicted to nicotine is covered as is a study of a compound that enhances memory in mice with Alzheimer-like symptoms. This issue also reports on research into treating mood disorders in drug abuse patients. The "NIDA Goes to School" campaign is described as well.

NIDA NOTES, Vol. 14, Issue 1

NCADI NN0035

Establishment of NIDA's National Drug Abuse Treatment Clinical Trials Network is highlighted in this issue, which also commemorates "NIDA's 25th Anniversary with a Special Report, "NIDA Marks 25 Years of Progress in Drug Abuse Research." The Director reflects on the next generation of drug abuse research with an emphasis on speeding the adoption of science-based drug abuse prevention and treatment programs in the Nation's communities. The Institute's collaboration with the National Cancer Institute to create tobacco research centers is also featured. Other articles look at teen drug use, the long-term effects of drug use, and the role of stress in drug abuse relapse.

Other Publications

Needle, R.N., Lambert, E.Y., Coyle, S., and Haverkos, H.W. "Drug Abuse and Infectious Disease." In: Ammerman, R.T., Ott, P.J., & Tarter, R. E. (Eds.). *Prevention and Societal Impact of Drug and Alcohol Abuse*. Mahwah, N.J.: Lawrence Erlbaum Associates, Inc., pp. 125-149, 1999.

In March, 1999, a special issue of *Clinics in Perinatology* was published on Prenatal Drug Exposure and Child Outcome. This special issue covers topics including historical trends in the research; mechanisms of action of the drugs; methodological considerations; status of knowledge about maternal and obstetrical effects, perinatal effects, early development, and longer-term outcomes; and intervention strategies for drug-exposed infants. Several NIDA-supported researchers were involved in the preparation of this volume, including Barry Lester, who was guest editor for the issue. The Foreword was prepared by Dr. Leshner, and one of the chapters was written by Vincent Smeriglio and Holly Wilcox (Center on AIDS and Other Medical Consequences of Drug Abuse [CAMCODA]).

De La Rosa, M.R., Segal, B., and Lopez, R.E., (Eds.) *Conducting Drug Abuse Research with Minority Populations: Advances and Issues*. Binghamton, NY: Haworth Press, Inc., 1999. Simultaneous publication as a monograph, *Drugs & Society* 14, 1/2, 1999.

Katz, J.K., Izenwasser, S., Kline, R.H., Allen, A.C., and Newman, A.H. Novel 3 -Diphenylmethoxytropane Analogs: Selective Dopamine Uptake Inhibitors with Behavioral Effects Distinct from those of Cocaine. *J. Pharmacol. Exp. Ther.* 288, pp. 302-315, 1999.

Vaughan, R.A., Agoston, G.E., Lever, J.R., and Newman, A.H. Differential Binding Sites of Tropane-Based Photoaffinity Ligands on the Dopamine Transporter. *J. Neurosci.* 19, pp. 630-636, 1999.

Preston, K.L., and Bigelow, G.E. Opioid Discrimination in Humans: Discriminative and Subjective Effects of Progressively Lower Training Dose. *Behavioural Pharmacology*, 9, pp. 533-543, 1998.

Asanuma, M. and Cadet, J.L. Methamphetamine-Induced Increase in Striatal NF-kappaB DNA-Binding Activity is Attenuated in Superoxide Dismutase Transgenic Mice. *Brain Res Mol Brain Res* 60(2), pp. 305-309, 1998.

Bolla, K.I., Cadet, J.L., and London, E.D. The Neuropsychiatry of Chronic Cocaine Abuse. *J Neuropsychiatry Clin Neurosci* 10(3), pp. 280-289, 1998.

Goodman, C.B., Heyliger, S., Emilien, B., Partilla, J.S., Yang, H.Y., Lee, C.H., Cadet, J.L. and Rothman, R.B. Regulation of Mu Binding Sites after Chronic Administration of Antibodies Directed Against Specific Anti-Opiate Peptides. *19(10)*, pp. 1703-9, 1998.

Haverkos, H.W., Turner, J.F., Jr, Moolchan, E.T., and Cadet, J.L. Relative Rates of AIDS Among Racial/Ethnic Groups by Exposure Categories. *J Natl Med Assoc.* 91(1), pp. 17-24, 1999.

Hayashi, T., Tsao, L.I., Cadet, J.L., and Su, T.P. [D-Ala2, D-Leu5]enkephalin Blocks the Methamphetamine-Induced C-Fos mRNA Increase in Mouse Striatum. *Eur J Pharmacol* 5;366 (2-3), 1999.

Tsao, L.I., Ladenheim, B., Andrews, A.M., Chiueh, C.C., Cadet, J.L. and Su, T.P. Delta Opioid Peptide [D-Ala2,D-leu5]Enkephalin Blocks the Long-Term Loss of Dopamine Transporters Induced by Multiple Administrations of Methamphetamine: Involvement of Opioid Receptors and Reactive Oxygen Species. *J Pharmacol Exp Ther* 287(1), pp. 322-331, 1998.

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National Institute on Drug Abuse

Director's Report to the National Advisory Council on Drug Abuse

May, 1999

Staff Highlights

Honors and Awards

Arthur MacNeill Horton, Jr., Ed.D., DCSR, has been appointed Chairperson of the ABPP Committee of the Division on the Psychology of Addictive Behaviors (50) of the American Psychological Association (APA).

Dr. David A. Gorelick, IRP, has been elected to fellowship in the American Psychiatric Association. He will be inducted as a fellow at the annual meeting May 17.

Dr. Amy Newman, IRP, was awarded scientific tenure - March 15, 1999.

Dr. Amy Newman, IRP, was awarded the 1998 Sato International Memorial Award by the Pharmaceutical Society of Japan in March 1999, Tokushima, Japan.

Gary Fleming, Chief, Grants Management Branch, OPRM, received a Special Recognition Award from the NIH Grants Management Community for his work on revising the NIH Grants Policy Statement. This award is given to those whose actions produce a positive and measurable outcome related to grants management.

Staff Changes

David Anderson joined the staff of PILB on February 16, 1999 and assumed the editorship of *NIDA NOTES*. Mr. Anderson has been Senior Editor of *RN*, a journal for nurses, and *Contemporary Internal Medicine*, for primary care physicians. He has also served as founding editor of *CV Nurse* and contributing editor to *Patient Care and Business & Health* magazines. Mr. Anderson has a master's degree in Population and International Health from Harvard School of Public Health, and has written original research and policy monographs on international issues in abortion, AIDS, male fertility, and Russian mortality for the International Union for the Scientific Study of Population. Other health-related organizations he has worked with include the Pan American Health Organization, Pathfinder International, Data for Decision-Making, and the Harvard Center for Population and Development.

Nathan Appel, Ph.D., has joined the Pharmacology and Toxicology Branch of the Medications Development Division. Dr. Appel received his Ph.D. in physiology from the University of Toronto and postdoctoral training in neuroanatomy and neuropharmacology at the University of Minnesota and the NIDA Addiction Research Center. Prior to joining MDD, Dr. Appel was employed by the FDA Center on Drug Evaluation and Research, Division of Applied Pharmacology Research, where he worked on developing methods to determine the neurotoxic effects of drugs. At MDD Dr. Appel will be responsible for developing a (meth)amphetamine treatment discovery program and directing the ongoing neurotoxicity screening program.

Michael Costa, formerly with the Administrative Office of the U.S. Courts joined NIDA's Grants Management Branch, OPRM, as a Grants Management Specialist on March 14, 1999. Mr. Costa has had a substantial amount of experience

in grants and contracts, largely at the Office of Naval Research, and will serve as the specialist for the Treatment Research Branch, the Services Research Branch, and CAMCODA.

Thomas F. Hilton, Ph.D., joined the Services Research Branch of the Division of Clinical and Services Research on March 1, 1999. Dr. Hilton, an organizational psychologist, formerly managed the FAA Training and Organizational Research Laboratory at the Federal Aviation Administration's Civil Aeromedical Institute in Oklahoma City, and conducted studies on organizational climate and managerial efficiency. At NIDA, he plans to develop research on organizational factors affecting the identification and implementation of therapeutic and managerial innovations in drug abuse treatment service delivery.

Michelle Muth joined the Public Information and Liaison Branch as Press Officer on April 25, 1999. Prior to coming to NIDA, Ms. Muth was Senior Press Officer at the Federal Trade Commission. Before that, she was Acting Director of Public and Legislative Affairs at the U.S. Office of Consumer Affairs, and she also served in the Division of Policy and Intergovernmental Affairs there. She received her M.A. from University College in Cardiff, Wales, and her M.B.A. from Marymount University in Virginia.

Robert Walsh, has accepted the position of Acting Chief of the Regulatory Affairs Branch in the Medications Development Division. Bob replaces Stephen Sparenborg, Ph.D. who has left to pursue a position with the private sector in Frederick Maryland. Mr. Walsh is certified by the Regulatory Affairs Professional's Society and is one of the founding members of the Medications Development Division.

Grantee Honors

Dr. Ronald Breslow from Columbia University is the recipient of the 1999 Priestley Medal, the American Chemical Society's most prestigious award for distinguished services to chemistry. Dr. Breslow's NIDA grant is a project that grew from his work on biometric approaches to catalysis. The purpose of the work is to design and synthesize a selective catalyst which binds to cocaine in vivo, and hydrolyzes it to inactive products. Such a catalyst would have potential uses as a treatment agent for cocaine toxicity and overdose. The catalysts being synthesized are cyclodextrins which act as enzyme mimics by binding to cocaine.

Dr. Ronald Kessler of Harvard University has been elected to the Institute of Medicine.

Dr. Ronald Kessler has also been selected as an Honorary Fellow of the American Psychiatric Association.

Dr. Lynn McDonald, University of Wisconsin, and developer of the Families and Schools Together (FAST) program, has been appointed to a three year term on the President's Advisory Council on Youth Drug Use. This is a 3 year appointment starting in 1999 and ending in 2002.

Dr. Christina Mitchell was honored by the American Journal of Community Psychology for her paper "The Structure of Problem and Positive Behavior among American Indian Adolescents: Gender and Community Differences." The paper was selected as one of the ten most significant studies published in that journal in its first 25 years and will be included in an anthology volume on methodological advances.

Dr. Howard Moss of the University of Pittsburgh was awarded a U.S. Speaker and Specialist Grant Award, Asuncion, Paraguay, U.S. Information Agency September, 1998. This award was provided to travel to Paraguay and engage in information exchanges with governmental and psychiatric professionals concerning the etiology of drug abuse and methods of drug abuse prevention.

Dr. Eric Nestler, Yale University School of Medicine, was recently elected to the Institute of Medicine. Dr. Nestler has made substantial contributions to research focusing on the brain's responses to repeated perturbations under both normal and pathological conditions. He has done important work to identify molecular changes that drugs of abuse produce in the brain to cause addiction, and to characterize the genetic and environmental factors that determine individual differences in the ability of the drugs to produce these changes.

Charles P. O'Brien, M.D., Ph.D., University of Pennsylvania School of Medicine, Philadelphia, PA, was voted 1999 President-Elect of the American College of Neuropsychopharmacology.

Dr. Thomas Wills of Yeshiva University has been nominated for a year in residency at the Center for Advanced Study in the Behavioral Sciences, Stanford, CA.

Dr. Mark Von Zastrow, Assistant Professor of Psychiatry and Cellular and Molecular Pharmacology, at the University of California, San Francisco received The Presidential Early Career Award for Scientists and Engineers. His work

played a major role in developing the current understanding of the mechanisms of protein sorting in the regulated secretory pathway. Dr. Von Zastrow made valuable contributions to the development of an RNA method for amplification from a small group of cells or a single cell, characterized the process of sequestration of an adrenergic receptor using immunocytochemical techniques, and identified the cellular proteins mediating sequestration. His current work concerns the regulated endocytic trafficking of G protein-coupled receptor systems and the identification of distinct membrane trafficking pathways that distinguish between and selectively mediate the movement of structurally homologous receptor proteins. His laboratory is working to identify and clone proteins that mediate these novel mechanisms, and to understand how these mechanisms interface with conserved machinery involved in other trafficking operations. Dr. Von Zastrow was the recipient of a Dana Fellowship in Neuroscience (1990-1992), a Howard Hughes Medical Institute Postdoctoral Fellowship for Physicians (1991-1993), and was named as NARSAD Young Investigator in 1994. He currently holds a Scientist Career Development Award and a FIRST Award from the National Institute on Drug Abuse.

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